

ARMY

PROPOSAL SUBMITTAL

The United States Army Research Office (ARO), reporting to the Army Research Laboratory (ARL) manages the Army's Small Business Technology Transfer (STTR) Program. The following pages list topics that have been approved for the fiscal year 2004 STTR program. Proposals addressing these areas will be accepted for consideration if they are received no later than the closing date and hour of this solicitation.

The Army anticipates funding sufficient to award one or two STTR Phase I contracts to small businesses with their partner research organizations in each topic area. Awards will be made on the basis of technical evaluations using the criteria contained in the solicitation, within the bounds of STTR funds available to the Army. If no proposals within a given area merit support relative to those in other areas, the Army will not award any contracts for that topic. Phase I contracts are limited to a maximum of \$100,000 over a period not to exceed six months.

Based upon progress achieved under a Phase I contract, utilizing the criteria in Section 4.3, a firm may be invited to propose on Phase II. Note that under the new Congressional Reauthorization for the STTR Program, any Phase II contracts following on Phase I proposals submitted under this solicitation will be limited to a maximum of \$750,000 over a period of two years. Contract structure for the Phase II contract is at the discretion of the Army's Contracting Officer after negotiations with the small business.

Please Note!

The Army requires that your entire proposal (consisting of Proposal Cover Sheets, the full Technical Proposal, Cost Proposal, and Company Commercialization Report) must be submitted electronically through the DoD SBIR/STTR Proposal Submission Website. A hardcopy is NOT required. Hand or electronic signature on the proposal is also NOT required.

The DoD-wide SBIR Proposal Submission system (available at <http://www.dodsbir.net/submission>) will lead you through the preparation and submission of your proposal. Refer to section 3.0 at the front of this solicitation for detailed instructions on Phase I proposal format. You must include a Company Commercialization Report as part of each proposal you submit however, it does not count against the proposal page limit. If you have not updated your commercialization information in the past year, or need to review a copy of your report, visit the DoD SBIR Proposal Submission site. Please note that improper handling of the Commercialization Report may result in the proposal being substantially delayed and that information provided may have a direct impact on the review of the proposal. Refer to section 3.4n at the front of this solicitation for detailed instructions on the Company Commercialization Report.

Be reminded that if your proposal is selected for award, the technical abstract and discussion of anticipated benefits will be publicly released on the Internet therefore, do not include proprietary or classified information in these sections. DoD will not accept classified proposals for the STTR Program. Note also that the DoD web site contains timely information on firm, award, and abstract data for all DoD SBIR Phase I and II awards going back several years. This information can be viewed on the DoD SBIR/STTR Awards Search website at www.dodsbir.net/awards.

ARMY 04 STTR Topic List

A04-T001	Interactive Terrain Analysis
A04-T002	Human-Computer Visualization
A04-T003	Biofilm Appliques for Corrosion Protection
A04-T004	Metal Organic Framework Adsorbents for Fuel-Cell Relevant Small Molecules
A04-T005	Imaging Infrared System With Extended Depth of Field Focusing
A04-T006	Development of New Production Technologies for Humanized Antibodies
A04-T007	Nanostructured Thermoelectric Composites
A04-T008	Fast Laser Pulse Shaping for Molecular Control and CB Detection
A04-T009	Neuromorphic Control System for Powered Limb Splints
A04-T010	Hypersensitive Detection of Unique Protein Signatures of Biothreat Agents
A04-T011	Morphology and Composition of Nanomaterials Based on Laser Microplasma Spectroscopy
A04-T012	High Power Mid-Wave Infrared (MWIR 3-5 Mmicron) Semiconductor Lasers
A04-T013	Biologically Inspired Acoustic Direction Finding for Soldiers
A04-T014	High-Resolution Near-Field Probe System for Microwave Circuit and System Design and Analysis
A04-T015	Terahertz-Frequency Quantum-Dot (THz QD) Lasers for Sensing & Communications
A04-T016	Smooth, Piecewise-Polynomial Terrain Representation Using Nontraditional Metrics
A04-T017	High Confidence Multimodal Biometric System
A04-T018	Rapid Assessment of Individual Soldier Operational Readiness
A04-T019	Tactical Biorefinery for Forward Fuel Production
A04-T020	Metabolomic Evaluation of Combat Personnel for Optimum Fitness and Performance
A04-T021	Hazardous Vapor Collection and Concentration for Spectral Sensing
A04-T022	Novel Nano-Structures for Multiplexed Micro-Array
A04-T023	Use of Shape Memory Alloys for Structural Energy Dissipation in Extreme Loading Events
A04-T024	Artificial Oxygen Carrier Solution for Small Volume Resuscitation
A04-T025	Automated Behavioral Health Triage
A04-T026	GPS-Based Tracking System for Trauma Patients
A04-T027	Development of Bioassays for Prion Infectivity Using Human, Deer, or Elk Cells
A04-T028	Portable Cell Maintenance System for Rapid Toxicity Monitoring

ARMY 04 STTR Topic Descriptions

A04-T001

TITLE: Interactive Terrain Analysis

TECHNOLOGY AREAS: Information Systems, Human Systems

ACQUISITION PROGRAM: PM, Future Force

OBJECTIVE: The purpose of this research is to investigate how Intelligent Tutoring Systems and/or Intelligent Agents can be utilized to provide decision support and training in battlespace analysis for people, and route instruction to robots. Accurate terrain and weather products, with great spatial and temporal detail will be a necessity for supporting network sensing, mission analysis and the military decision making. These products need to be fused with intelligence information regarding friendly, enemy, and noncombatant positions in the battlespace. Current terrain analysis tools display information to a human user through graphical visual displays; but it is up to the user to ask the analysis tool for the right information, and to interpret and apply the results of the analysis in planning. Fusion of the terrain information and intelligence information must be performed in the soldier's head. The purpose of this research is to produce a sub-system that will support the soldier through terrain analysis and route planning, with a tool that integrates terrain and intelligence information. In addition, that sub-system can also be used to guide the movement of robotic platforms. If an intelligent agent or tutor can be "informed" of mission intent, it should also be able to provide dynamic guidance as the mission unfolds, by taking into account changes in the battlespace as they occur.

DESCRIPTION: Given that the Objective Force will make use of robotic platforms, these platforms will have to be guided through space, via instructions provided by human operators, automated intelligent agents, or a combination of the two. Current digitized Command and Control (C2) systems, as well as simulation training tools (e.g., One-SAF Testbed [OTB or OOS]), incorporate terrain analysis tools that provide visual output to a human observer to aid maneuver; however, the human is responsible for asking for the right analysis and interpreting that output on his/her own. The purpose of this research is to take an existing system with terrain analysis capabilities and show how it can be modified such that instead of merely outputting a digital display, it sends information to (1) an intelligent agent or intelligent tutoring system that will guide a human user in route planning and mission execution, and (2) a simulated robotic entity, so as to guide its tactical movement throughout its assigned mission.

In order to achieve unprecedented momentum, and freedom of maneuver, the Objective Force must see the complete picture of the operating environment, in all of its aspects. Further, the Objective Force must have an understanding of this picture that allows it to take away the enemy's "home court advantage" and give our leaders a better understanding of the environment than our adversaries. Current terrain analysis tools fail to link intelligence information and terrain information. The user must do this manually, through the types of analyses requested of the system. A more intelligent analysis tool would query the user as to mission intent, and itself integrate intelligence, terrain, and other available relevant information to provide alternative solutions meeting the intent.

With current systems, the output from terrain analysis tools is static. Once the analysis is completed it is "closed," and not updated unless the operator makes a specific request. However, given the anticipated capabilities of the Future Combat System to keep a near real time operating picture, there is the potential to update data on intervisibility as a mission unfolds and platform positions (both friendly and enemy) change. If an intelligent agent or tutor can be properly informed of mission intent, it should have the ability to provide relevant dynamic terrain and intervisibility guidance to both human operators and robotic platforms.

The lessons learned from this research will be invaluable in developing an integrated Future Combat System in which human operators can make the best use of the tools available, make well-informed dynamic re-planning decisions, and understand and anticipate the behavior of their robotic partners.

PHASE I: This is a 6-month effort to test the scientific, technical and commercial merit and feasibility of a particular concept.

- Research terrain analysis facilities in newest available version of One-SAF-Testbed (SAIC, 2003), and Force XXI Battle Command Brigade and Below (FBCB2 3.4, 2001; Stottler & Pike, 2002) with particular attention to how the computational output of the terrain analysis features of these systems can be captured and utilized. Examine how the user interfaces can be modified to provide a mixed-initiative interchange with an intelligent agent or tutor.
- Evaluation of the ease of modification of the systems examined and selection of system for modification.
- Investigation of tactically realistic movements required in projected Objective Force missions and ways for capture of mission intent by intelligent agent.
- Examination and description of how terrain analysis data can be integrated with intelligence information (e.g., enemy positions), to produce maneuver planning guidance to human operator or robotic platform.
- Examination and description of required mixed-initiative communications between an intelligent agent or tutor and a human operator, to guide route planning and execution.
- Examination and description of required communications between intelligent agent and simulated robotic entity, to guide

robotic tactical movement.

- Examination and description of terrain database requirements, including possibilities for user/sensor updating of terrain database in real time.
- Design architecture for required intelligent agents and system modifications.

The projected outcome of Phase I will be a research report detailing the above items, as well as a plan for a prototype to be delivered during Phase II.

PHASE II research efforts will include:

- Building the prototype designed in Phase I
- Testing the prototype with a reconnaissance mission with Ft. Polk database.
- Demonstrating the ability of the prototype to provide route planning guidance (and training) to human operators.
- Demonstrating the ability of the prototype to task a simulated robotic platform with tactically realistic movement.
- Demonstrating that a human operator trained with the prototype has a better ability to understand and predict the behavior of the simulated robotic platform than an operator not trained with the prototype.
- Demonstrating the ability of the prototype to provide human operator and robot with relevant dynamic information as simulation scenario changes enemy platform positions.
- Conducting Usability analysis of the prototype, to determine reaction by operators.
- Developing a detailed report on lessons learned during the effort and suggestions for improvement.

The Phase II deliverables will be demonstrations of the prototype, experimentation with human operators, and a detailed research report outlining findings.

PHASE III DUAL USE APPLICATIONS: In Phase III, it is anticipated that the successful bidder will be able to market this prototype to the lead system integrator for FCS, as well other branches of the military. Phase III should include validation with military experts to evaluate tactical goodness of route planning guidance. In addition, a generalization of the concept of the tool to other forms of data analysis for planning and execution in dynamic situations (i.e., not just terrain analysis and intervisibility) could open up a wide range of possibilities. For example, the system could be extended to cover weapons range analysis. In the nonmilitary arena, the prototype could be extended for the use of control of robotic tasking in dynamic situations such as search and rescue.

REFERENCES:

2003 U.S. Army Posture Statement <http://www.army.mil/aps/2003/realizing/transformation/operational/objective/index.html>

Burmester, G.M., Stottler, D., & Hart, J. (2002). Embedded training intelligent tutoring systems (ITS) for the future combat systems (FCS) command and control (C2) vehicle. Proceedings of the Interservice/Industry Technology, Simulation, and Education Conference, Orlando, FL.

FBCB2 3.4 (2001). <http://filasat.hood.army.mil>

Gray, R.S. (2000) Soldiers, Agents and Wireless Networks: A Report on a Military Application. Proceedings of the Fifth International Conference and Exhibition on the Practical Application of Intelligent Agents and Multi-Agents, Manchester, England.

Objective Force Task Force (2002). The Objective Force in 2015 White Paper. [http://www.objectiveforce.army.mil/pages/OF%20in%202015%20White%20Paper%20\(final\).pdf](http://www.objectiveforce.army.mil/pages/OF%20in%202015%20White%20Paper%20(final).pdf)

Rhea, J. (2003). The next 'new frontier' of artificial intelligence. Military and Aerospace Electronics. http://mae.pennnet.com/Articles/Article_Display.cfm?Section=Archives&Subsection=Display&ARTICLE_ID=86890

SAIC website (2003). OneSAF Testbed Baseline (OTB) <http://www.asset.com/solutions/simsystm/otb.html>

Schafer, R. (2003). Robotics to play major role in future warfighting. USJFCOM, <http://www.jfcom.mil/newslink/storyarchive/2003/pa072903.htm>

Sparshat, R. and Justice, N. (2003). Future Battle Command and Control System. Army Science Conference, Orlando, FL. Abstract available at: http://www.asc2002.com/Abstracts_only/o/OA12.pdf

Stottler, R.H. and Pike, B. (2002). An embedded training solution: FBCB2 tactical decision making intelligent tutoring system. Proceedings of the Interservice/Industry Technology, Simulation, and Education Conference, Orlando, FL.

Vasandani, V. & Govindaraj, T. (1991). An experimental evaluation of an intelligent tutor for diagnostic problem solving. In L.

Birnbaum (Ed.), The International Conference on the Learning Sciences, Charlottesville, VA: Association for the Advancement of Computing in Education, 1991.

KEYWORDS: Terrain analysis, intervisibility, route planning, training, robotic platform, intelligent tutor, intelligent agent, maneuver

A04-T002

TITLE: Human-Computer Visualization

TECHNOLOGY AREAS: Human Systems

OBJECTIVE: Design and build a system to augment and complement human-computer visualization capabilities.

DESCRIPTION: Advances in digital- and bio-technology are resulting in a convergence of human-computer capabilities. Much of the current research, however, targets the ability of computers to augment human action, such as brain-machine interfaces(1). Important but neglected research areas include the ability of computers to augment and complement human perception and cognition, including to train and support human visualization and conceptualization skills(2). The Army's requirement to See First relies heavily on sensor-driven computer depictions of a Common Operational Picture (COP) to empower battle command visualization (3). This STTR topic requires application and extension of current technologies to match user and system representations of real world environments, such as the COP. The technology will recognize system representations of battlefield patterns and situations depicted on the COP and identify and highlight state changes particularly changes induced by dynamic sensor inputs. The technology will recognize human perceptual and cognitive representations of battlefield patterns and situations to ensure the state changes identified and highlighted on the COP are considered meaningful from a human perspective. As a result, the technology will apply its "understanding" of human and system representations to mutually shape and complement human-computer visualization capabilities.

PHASE I: Design and develop a system to recognize and correlate human and computer representations of battlefield patterns and situations including specification of encoding and decoding processes for perception, cognition and digital visualization technologies.

PHASE II: Develop and demonstrate a prototype system that augments and complements human and computer representations, including the ability to train human and computer visualization capabilities. Conduct testing to prove feasibility in realistic and complex operating conditions.

PHASE III DUAL USE APPLICATIONS: This system could be used in many computer-mediated environments including military, security, business, manufacturing, marketing, and education.

REFERENCES:

1 Brain Machine Interfaces, Defense Advanced Research Projects Agency. Available online at: <http://www.sciencedaily.com/releases/2002/08/020820071329.htm>

2 Morrison, J.G., Kelly, R.T., Moore, R.A., & Hutchins, S.G. (1998). Implications of decision-making research for decision support and displays. In Making Decisions Under Stress: Implications for Individual and Team Training, edited by J.A. Cannon-Bowers, and E. Salas. American Psychological Association: Washington, DC, 91-113.

3 U.S. Department of the Army. (2003). Mission Command: Command and Control of Army Forces (Field Manual 6-0). Headquarters, Department of the Army.

KEYWORDS: Perception, cognition, pattern recognition, neural imaging, training, performance support.

A04-T003

TITLE: Biofilm Appliques for Corrosion Protection

TECHNOLOGY AREAS: Ground/Sea Vehicles, Materials/Processes

OBJECTIVE: Design a polymer-based, flexible appliqué system that carries and supports a biofilm that will protect an aluminum airframe structure from corrosion. The appliqué must meet the adhesion requirements of current commercial aircraft appliques and must be capable of supporting the biofilm autonomously for 48 hours in outdoor weather conditions similar to those of the Aberdeen Proving Grounds in May (24C high, 12C low, 18C median, 80%RH, indirect sunlight).

DESCRIPTION: Corrosion control and repair costs the DoD over \$1B/yr. The development of an effective, self-repairing corrosion protection system could, therefore, have a significant return on investment. Biofilms, which by their nature are

adherent, self-repairing systems, can offer such a possibility. Microorganisms have long been known to affect the corrosion of structural metals (termed microorganism influenced corrosion of MIC). Recent research has also shown that the component microorganisms of biofilms can be genetically engineered to significantly reduce corrosion rates in brasses and steels, and to reduce attack of structural aluminum alloys. These organisms work by at least three different mechanisms: consuming oxygen near the metal surface; secreting polypeptides that chelate with the corrosion by-product ions to coat and protect the surfaces; secreting anti-microbial polypeptides that kill corrosion-promoting microorganisms. Some biofilm organisms have even been patented for corrosion protection. The literature examples, however, are all continuously immersed in water to maintain the integrity of the biofilm. Any application to a real system would involve having the biofilm maintained in a nominally dry setting and subject to mechanical stress and abrasion. Having a flexible polymer-based appliqué to support the biofilm structurally, protecting it from direct sunlight, and retaining sufficient moisture to allow the biofilm to survive without being completely immersed, only periodic wettings, would allow the technology to be used in military ground and air vehicles as a general corrosion protection system.

PHASE I: Identify candidate biofilm system and verify corrosion inhibition effect. Design polymer appliqué film to support biofilm while also allowing nourishment of biofilm and sufficient contact with the base metal surface to provide action. The biofilm may also provide the adhesion action, though that is not a requirement of the project.

PHASE II: Develop and demonstrate a prototype system in a realistic environment, using both laboratory and tests of simulated rotocraft airframe structures. In addition, conduct testing to verify feasibility of the basic concept over an extended operating time on a simulated rotocraft airframe structure.

PHASE III DUAL USE APPLICATIONS: The appliqué system should be used in a broad range of military and civilian applications where corrosion protection is required. Specific examples are protection of ground vehicles such as the High Mobility Multi-purpose Wheeled Vehicle (HMMWV), inhibition of ship-board corrosion.

REFERENCES: A. Jayaraman, Appl. Microbiol. Biotechnol. 52 (1999) 787-790; D. Ornek et al., Corrosion Sci. 44 (2001) 2291-2302; D. Ornek et al., Appl. Microbiol. Biotechnol. 58 (2002) 651-657.

KEYWORDS: Biofilms, Microorganism Influenced Corrosion, MIC, Corrosion Protection, Appliqués

A04-T004

TITLE: Metal Organic Framework Adsorbents for Fuel-Cell Relevant Small Molecules

TECHNOLOGY AREAS: Ground/Sea Vehicles, Materials/Processes

OBJECTIVE: Design and develop robust metal-organic framework (MOF) materials that selectively remove small molecule contaminant(s) produced by a fuel cell's fuel processing system. Package MOF material as a component in a compact fuel processing system sufficient to support a polymer electrolyte membrane 20-W fuel cell for 72 hours. Target minimum energy density for the fuel processing system, including fuel, is 1.5 kWh/kg or 90 g of hydrogen per kg of system weight.

DESCRIPTION: The Army has need for high-energy density, lightweight power sources for the soldier; for example, one potential scenario would require 20 W (electric) for a three-day mission. Hydrogen-air polymer electrolyte membrane fuel cells (PEM FCs) are candidates to fill this need, but the source of hydrogen is problematical. Hydrocarbons and ammonia are energy-dense compounds that after chemical transformation can provide the necessary hydrogen. The PEM FC electrocatalysts, however, are susceptible to poisoning from small molecules produced in the fuel processor, e.g., CO, H₂S, or unreacted ammonia, which must be removed prior to feeding the product gas to the FC. Adsorption is a potential technology to remove these unwanted components but highly efficient and selective adsorbents are required. Recently, a novel crystalline nanoporous material has been reported that consists of metal atoms occupying the vertices of a lattice, with the lattice size, porosity, and chemical environment defined by the organic linker molecules that bind the metal atoms into a robust periodic structure (1). These so-called metal-organic framework (MOF) materials have been demonstrated as adsorbents for methane (2) and hydrogen (3). The ability to molecularly engineer the lattice size, chemical environment, and possibly structure by judicious choice of the metal centers and organic linkers offers the opportunity to develop adsorbents of potential utility for contaminant removal in hydrocarbon or ammonia fuel processors.

PHASE I: Design, synthesize, characterize, and evaluate MOF materials that may selectively remove small molecule contaminant(s) generated in a PEM FC fuel processor. Measure adsorption isotherms of small molecule contaminant(s) on the MOF materials over temperature and pressure ranges relevant to a compact power system. Determine reversibility and chemical stability of the MOF materials over these same temperature and pressure ranges. Report a conceptual design using the MOF materials as a component of a compact fuel processing system to supply a 20-W PEM FC and assess quantitatively whether SOA technology is improved.

PHASE II: Design, construct, and evaluate a compact PEM FC fuel processing system in which the MOF material is an integral

component. The fuel processor must supply contaminant-removed hydrogen at a rate sufficient to support a 20-W PEM FC for 72 hours. Deliver a packaged compact fuel processing system to the DoD. Target minimum energy density for the fuel processing system, including fuel, is 1.5 kWh/kg or 90 g of hydrogen per kg of system weight.

PHASE III DUAL USE APPLICATIONS: Developments in fuel processors for fuel cells will have immediate impact on a wide range of military uses as well as commercial power sources such as computer power, emergency medical power supplies, recreational power, etc...

REFERENCES:

1. M. Eddaoudi, D. Moler, H. Li, B. Chen, T. Reineke, M. O'Keeffe, and O. Yaghi, "Modular Chemistry: Secondary Building Units as a Basis for the Design of Highly Porous and Robust Metal-Organic Carboxylate Frameworks," *Acc. Chem. Res.* 2001, 34, 319-330.
2. M. Eddaoudi, J. Kim, N. Rosi, D. Vodak, J. Watcher, M. O'Keeffe, and O. Yaghi, "Systematic Design of Pore Size and Functionality in Isoreticular MOFs and Their Application in Methane Storage," *Science*, 2002, 295, 469-472.
3. N. Rosi, J. Eckert, M. Eddaoudi, D. Vodak, J. Kim, M. O'Keeffe, and O. Yaghi, "Hydrogen Storage in Microporous Metal-Organic Frameworks," *Science*, 2003, 300, 1127-1129.

KEYWORDS: Adsorbents, metal-organic framework, fuel cells, fuel processors

A04-T005

TITLE: Imaging Infrared System with Extended Depth of Field Focusing

TECHNOLOGY AREAS: Ground/Sea Vehicles, Sensors, Electronics, Battlespace

OBJECTIVE: Develop innovative optical detection and imaging system that will allow battlefield imaging through smoke, dust, and fog obscuring in the 10 micron wavelength range.

DESCRIPTION: For seeing through dust, smoke screens, and fog, the use of 10 micron radiation instead of visible light is an excellent option, but the biggest difficulty is that thermal radiation sources are fairly low and to see 10 miles, one needs prohibitively large optics. For example dishes several meters in diameter would be required. For example, one might use low cost gas (e.g. CO₂) and/or solid-state lasers that operate at 10.6 microns as sources of illumination. The use of a narrow band far infrared source is a big advantage in the system since one can use a narrow pass filter to cut out stray illumination as well as spurious thermal radiation. With these searchlights remotely located the battlefield becomes well illuminated. This topic seeks the development of innovative, small portable telescopes using an uncooled array of detectors that can be used to give excellent viewing potential from 1 to 10 miles through all types of haze, keeping the entire field in focus. It may be necessary to use adaptive optic techniques to remain in focus over the entire 1 to 10 mile range.

PHASE I: Develop a feasibility concept for an imaging system that can effectively operate through obscuring typical of battlefield conditions.

PHASE II: Build and demonstrate a prototype imaging system, develop guidelines for field tests.

PHASE III DUAL USE APPLICATIONS: Build, manufacturable, and deliver prototypes to Army lab scientists and document/demonstrate effectiveness in field tests. Implementation of portable field deployable units operating in mock battles. For dual use, show system application for commercial airports or traffic control.

REFERENCES: N.S. Kopeika, "Imaging in adverse environments," OSA Annual Meeting, Santa Clara, CA, September 1999.

N. George, C. J. Ditchman, and Xi Chen, "Digital recovery for images degraded by turbulence," OSA Annual Meeting, Santa Clara, CA, September 1999.

KEYWORDS: Imaging, obscuring, IR, Laser

A04-T006

TITLE: Development of New Production Technologies for Humanized Antibodies

TECHNOLOGY AREAS: Chemical/Bio Defense, Biomedical

DESCRIPTION: The majority of proteins approved for human use by the FDA are antibodies. Antibodies are a basic and powerful tool, and their uses include treatment of viral infections, bacterial infections, superantigen exposure, cancer, and

autoimmune diseases. However, antibodies obtained from normal animals can only be used once, due to the immuno-reactivity of the non-human components. Antibodies from other humans are often in limited supply, especially for biowarfare agents such as smallpox and anthrax where limited human exposure has occurred and it would be unethical to expose humans to the agent. In addition the use of proteins from other humans involves inherent risks of transmitting human diseases such as hepatitis and HIV. New or unknown bacteria or viruses also present obvious supply problems.

The development of a “humanized” mouse, in which the mouse antibody genes are inactivated and functionally replaced with human antibody genes, has recently been described. These humanized mice still exploit the high diversity and high specificity capacities of the natural immune system, but produce antibodies that are fully functional in humans. Ten such humanized antibodies produced in mice have entered clinical trials since 1998 and more are in preclinical testing.

This topic seeks to fund the development of second generation biosystem for production of fully humanized antibodies. Such a biosystem might be a larger mammal such as pig, goat, or horse. Development of a larger host animal would enable one animal to produce sufficient antibodies to protect the entire country against a particularly biowarfare or infectious disease agent. Quality and efficacy would be uniform, as all the antibodies would be derived from the same animal.

PHASE I: Begin construction of a transgenic animal system that will be capable of producing fully humanized antibodies. Host immunoglobulin genes would be removed and replaced by the corresponding human immunoglobulin genes.

PHASE II: Finish development of a transgenic animal system that is capable of producing high volumes of fully humanized antibodies. The finished animals will have their immunoglobulin genes replaced by human immunoglobulin genes. Proper rearrangement of human genomic immunoglobulin gene sequences will be demonstrated. The ability to produce antibodies with high specificity and high efficacy will be demonstrated.

PHASE III DUAL USE APPLICATIONS: DoD: Development of a variety of humanized antibodies to effectively counteract and prevent mortality and loss of troop efficacy from biowarfare agents and infectious diseases. Civilian: Development of a variety of humanized antibodies for prevention and treatment of viral and bacterial diseases, cancer, and autoimmune diseases.

REFERENCES:

Davis CG, Gallo ML, Corvalan JR. Transgenic mice as a source of fully human antibodies for the treatment of cancer. (1999) Cancer Metastasis Rev. 18(4):421-5.

Green, LL. (1999) Antibody engineering via genetic engineering of the mouse: XenoMouse strains are a vehicle for the facile generation of therapeutic human monoclonal antibodies. Journal of Immunological Methods 231 11-23.

Jakovovits, A. (1998) Production and selection of antigen-specific fully human monoclonal antibodies from mice engineered with human Ig loci. Advanced Drug Delivery Reviews Vol. 31, pp: 33-42.

Mendez M, Green, L, Corvalan, J, Jia X-C, Maynard-Currie, C, Yang, X-D, Gallo, M, Louie, D, Lee, D, Erickson, K, Luna, J, Roy, C, Abderrahim, H, Kirschenbaum, F, Noguchi, M, Smith, D, Fukushima, A, Hales, J, Finer, M, Davis, C, Zsebo, K, Jakovovits, A. (1997) Functional transplant of megabase human immunoglobulin loci recapitulates human antibody response in mice. Nature Genetics Vol. 15, pp: 146-156.

Yang XP, Gallo M, Ngan I, Nocerini M, Chen MM. Use of CMFDA and CMTMR fluorescent dyes in FACS-based antibody screening. Biotechniques 2002 Mar;32(3):678-80, 682.

KEYWORDS: Humanized antibodies

A04-T007

TITLE: Nanostructured Thermoelectric Composites

TECHNOLOGY AREAS: Materials/Processes

OBJECTIVE: Develop and demonstrate new bulk materials that derive significant enhancements in their thermoelectric performance through the introduction of quantum confined structures (precipitates or clusters). This program is directed at vastly improving the efficiencies of existing thermoelectric refrigeration and cryogenic cooling systems.

DESCRIPTION: Theoretical predictions (1,2) suggesting that large improvements in thermoelectric performance of semiconductor systems can be obtained in nanostructured composite systems have been confirmed recently in thin-film experiments. Record ZT (figure of merit) values have been demonstrated in PbTe-based quantum-well and quantum-dot systems prepared by MBE (3,4), and in BiTe-SbTe quantum-well systems prepared by MOCVD (5). The results affirm the efficacy of invoking quantum confinement effects and bandgap engineering concepts to fine tune the density of states and mobility of the

carriers as a means of significantly enhancing thermoelectric performance. In addition, the nanostructural character of the systems can degrade the lattice thermal conductivity of the material system by increasing phonon scattering at the various interfaces and atomic mass discontinuities. This combination of optimized band structure, higher electronic mobility and lower thermal conductivity directly translates into large (2-3 fold) enhancements in the overall thermoelectric figure of merit (ZT) of these systems. However, these gains have only been demonstrated in thin-film systems. To become commercially viable new low-cost processing routes are needed for preparing bulk materials that contain a nanostructured, thermoelectrically active component. To accomplish this objective, innovative new approaches to bulk materials processing are being sought, which are amenable to the development of nanostructured thermoelectric composites. Possible processing routes might include, for example, second phase precipitation of quantum dots within a semiconductor crystal, or dual-phase (core/shell) semiconductor nanopowder synthesis and consolidation, or the decoration of conductive polymer systems with thermoelectrically active clusters.

PHASE I: Investigate innovative processing approaches for obtaining bulk thermoelectric materials that derive significant enhancements in their thermoelectric performance through the introduction of a high density of quantum confined structures (quantum dots or nanowires) distributed within a semiconductor or polymer matrix.

PHASE II: Continue with development of the bulk thermoelectric materials. Demonstrate materials ZT values in excess of 2. Fabricate and test a prototype thermoelectric cooler system to demonstrate the overall efficiency of the system. Explore major cost and reliability issues associated with producing a material suitable for construction of a commercially viable cooling unit.

PHASE III DUAL USE COMMERCIALIZATION: This effort is intended to lead to the development of new materials with large potential ZT enhancements. This would provide efficient thermoelectric coolers to temperature below 100 K for cryogenic sensor and electronic applications, and would permit the direct substitution of all current CFC-based air conditioning and refrigeration technologies by thermoelectric cooler systems with plug compatible efficiencies. This technology would have immediate application to the commercial air conditioning, refrigeration and waste-heat recovery industries. It might also make feasible cryogenic electronics and computing, affording new opportunities for implementing device concepts based on superconductivity and other low temperature phenomena.

REFERENCES:

- (1) L.D. Hicks and M.S. Dresselhaus, Phys. Rev. B47 (1993), p. 12727-31;
- (2) L.D. Hicks and M.S. Dresselhaus, Phys. Rev. B47 (1993), p. 16631-34;
- (3) L.D. Hicks, T.C. Harman, X. Sun and M.S. Dresselhaus, Phys. Rev B, Vol 53, No. 16, (1996) 10493-96;
- (4) T. C. Harman, P.J. Taylor, D.L. Spears and M.P. Walsh, J. Electron Mater. Ltt. 29, L1 (2000);
- (5) R. Venkatasubramanian, E. Siivola, T. Colpitts and B. O'Quinn, Nature 413, 597-602 (2001).

KEYWORDS: Thermoelectric, quantum confinement, composite nanostructures, and bulk processing.

A04-T008

TITLE: Fast Laser Pulse Shaping for Molecular Control and CB Detection

TECHNOLOGY AREAS: Chemical/Bio Defense, Materials/Processes, Sensors

OBJECTIVE: Develop design of and hardware for closed-loop control of molecular motion by coherent electromagnetic fields. System will not include laser source or molecular detector. System will include fast, complex laser pulse shaping (phase and amplitude spatial light modulators and adaptive algorithm control system).

DESCRIPTION: DOD supported theoretical work, mostly by Rabitz at Princeton University during the past 15 years, has established the field of coherent control of molecular motion using shaped laser pulses. Experiments performed in several countries have validated those theoretical concepts. The experimental systems are now available only in a few specialized university laboratories. This technology will enable a wide range of applications, many of which likely have not been predicted. Sensitive, selective detection of chemical and biological threat agents is one application now being explored with support from the DOD Multiinvestigator University Research Initiative. This technology, if successful, will enable detection of threats in a complex background (dust, diesel exhaust, etc.) and may enable detection of previously unknown threats based on their toxicity. The control apparatus will provide the link between the laser source and the detector.

PHASE I: Design and assemble breadboard system and demonstrate molecular control, e.g., enhance selected decomposition channel or other clear evidence for control.

PHASE II: Design and build system with following attributes: compact, economical, and rugged. System should be compatible with portable laser systems and detectors suitable for field use. System should include reliable means for calibration and be

operable for at least one week without maintenance.

PHASE III: This equipment will have a wide range of applications for field detection (e.g., chemical and biological threats, explosives, toxic industrial chemicals). This methodology (in the lab) will also enable a broad range of fundamental studies of molecular properties.

REFERENCE: 1. Closing the Loop on Bond Selective Chemistry using Tailored Strong Field Laser Pulses, Levis, R.J., Rabitz, and H. J. Phys.Chem. Feature article 106, 2002, 6427 (119 references in this review)2. Evolutionary algorithms and their application to optimal control studies", D. Zeidler, S. Frey, K.L. Kompa, and M. Motzkus, Phys. Rev. A 64, 02342020

KEYWORDS: Molecular control, laser pulse shaping, learning algorithms, chem/bio detection

A04-T009

TITLE: Neuromorphic Control System for Powered Limb Splints

TECHNOLOGY AREAS: Biomedical

OBJECTIVE: Develop an analog control system based on neuromorphic principles to sense and control an active, light-weight, powered splint system for the lower limb, designed to permit useful walking in an individual with non-functional or damaged gastrocnemius/soleus (calf) muscles and/or severe tibial/fibular (shin) fractures that normally would prevent both weight bearing and mobility.

DESCRIPTION: The concept of exoskeletal enhancement of human limbs for both teleoperation as well as strength enhancement, termed the "waldo" by Robert Heinlein who published it as science fiction in 1942, has been an engineering research goal for some time. Modern implantations of augmented limb technology use control systems that are digital in nature and as a result are both computationally expensive, large and can be ill-fitted to intuitive human use without large scale engineering efforts. The emerging fields of neuro-ergonomics and neuromorphics harvest the analog designs nature has provided in existing biological nervous systems for sensing, feedback and control of physical systems, e.g. limbs, visual sensors. Neuromorphic systems may be simpler in computational design, smaller, more efficient and more suited as control devices to enhance or replace normal musculoskeletal function. Most current limb augmentation devices for use with lower leg trauma are passive systems (splints), that while light-weight, and capable of transferring up to 90% or more of the weight load from above the damaged area to the ground, depend on functional musculature and architecture of the remaining limb to permit mobility. The research requested here is to develop a combination portable (lightweight, small) control system, physical framework and actuators for external application to one leg of a non-amputee human being that not only mimics normal knee, ankle and foot action, but uses biomimetic methods and algorithms for using reflex feedback and central pattern generation as control inputs to allow actual walking. It can use as data environmental cues (gravity, orientation, weight, pressure, acceleration, timing, etc.), or it can additionally use some subset of bioelectric potentials (e.g. hip and /or leg muscle activity) if such can be detected non-invasively. Further developments of this control system are applicable to a range of mechanisms from powered battlefield armors to remote construction and loading devices that close the gap between the human and the task to actual prosthetics.

PHASE I: Develop a compact low-power neuromorphic circuit system that can sense both itself and the environment and pattern demand-based walking motions for an articulated and powered lower limb splint. This circuit will be mated to any convenient splint system selected or developed by the researcher, and demonstrated on an uninjured human test subject. Bilateral development and application is not ruled out, but is only a minor goal at this phase.

PHASE II: Further develop and demonstrate application of this system to a purpose-developed portable and optimized light-weight exoskeletal splint system on actual human volunteers who are lower limb amputees wearing non-motorized anatomically realistic prostheses. Additionally, create and demonstrate a two-legged system for bilateral use.

PHASE III DUAL USE APPLICATIONS: Beyond the obvious medical uses in limb trauma remediation, this system could be used in a broad range of military and civilian applications where augmentation of normal human movement, strength and function is desired.

REFERENCES:

Jung R, Brauer EJ, Abbas JJ. Real-time interaction between a neuromorphic electronic circuit and the spinal cord. IEEE Trans Neural Syst Rehabil Eng. 2001 Sep;9(3):319-26.

Higgins CM. Sensory architectures for biologically inspired autonomous robotics. Biol Bull. 2001 Apr;200(2):235-42.

Cymbalyuk GS, Patel GN, Calabrese RL, DeWeerth SP, Cohen AH. Modeling alternation to synchrony with inhibitory coupling: a neuromorphic VLSI approach. Neural Comput. 2000 Oct;12(10):2259-78.

KEYWORDS: Neuroergonomics, neuromorphic, analog controls, reflexes, anatomy, robotics, trauma, functional augmentation, bionics, prostheses, splints.

A04-T010

TITLE: Hypersensitive Detection of Unique Protein Signatures of Biothreat Agents

TECHNOLOGY AREAS: Chemical/Bio Defense

OBJECTIVE: The objective of this STTR is to develop a rapid, specific, innovative, and hypersensitive method for detecting and identifying unique protein biosignatures of biothreat agents

DESCRIPTION: In an intentional release of a microbial biothreat agent or toxin, the rapid, specific detection and identification of the threat is critical for minimizing the number of casualties that result. While a variety of presumptive tests are available for many agents, currently substantial manipulation and preparation time are required for specifically identifying the agent. Since all biothreat agents, viruses, bacteria, fungi, or toxins, have protein associated with them, tests identifying unique protein signatures of each agent could minimize the preparation time and effort in making a specific identification. However, most methods of protein detection require a substantial amount of the protein for analysis. This STTR seeks to develop an innovative approach for the separation and identification of unique biosignature proteins at near attomole levels, starting with complex protein mixtures as would be anticipated from environmental or tissue samples.

The technology to be developed under this STTR would have military and civilian importance. Many techniques for identifying biothreat agents rely on DNA technology. This usually entails a PCR-based regimen of amplification prior to identification. Having the correct primers for amplification for many different agents and having the equipment and trained personnel for the process is a daunting challenge. In addition, some viruses have RNA as their nucleic acid material and, of course, toxins would be expected to have neither. Thus, a protein-based technology could have enormous potential, if it is sufficiently sensitive and specific for the agents. While organisms could be engineered to be resistant to the usual antibiotics for controlling that organism, it is highly unlikely that the unique protein biosignatures for that agent would be altered. Furthermore, an appropriate separation and display technology could be used in probing for a number of different threat agents.

The technology that would result from this STTR could have many applications in a wide variety of fields. For example, the technology could be developed and modified for the areas of epidemiology, diagnostics, food and water contamination, forensics, agriculture, and many others.

PHASE I: With the collaboration of protein chemists, molecular biologists, and engineers, the basic technology for the separation and detection would be assembled and tested. Proof of principle could be achieved with known, purified proteins. Limits of sensitivity would be determined and compared with known techniques. Because the amount of the proteins in disseminated threats would be low, emphasis should be placed on sensitivity, reliability, and minimization of false positive reactions. Detection systems would be tested and calibrated. Theoretical limits of detection would be calculated and the criteria utilized for those calculations specified. Comparisons would be made with known systems.

PHASE II: A fully functional system would be developed, tested, and thoroughly documented to meet the limits of detection with specific biothreat agents or their surrogates. Technology would be perfected toward miniaturization, field deployability, and enhanced sensitivity. Field, water, and tissue samples would be tested with known gradients of surrogate proteins. Alternative detection systems would be analyzed using different probes such as antibodies, DNA and/or RNA aptamers, unique fluorescence, etc, to increase sensitivity and reliability. It is anticipated that at the end of Phase II a fully functional and field deployable unit would have been developed and shown to meet specifications under normal operating conditions.

PHASE III: DUAL USE APPLICATIONS: The separation and detection system would be modified and tested for a variety of field applications. The generality and efficacy of the technology in a multitude of military and civilian applications would be tested. In collaboration with the appropriate Army laboratories, potential biothreat agents would be tested in a variety of field simulations.

REFERENCES

Cordwell, S.J. 2002 Acquisition and archiving of information for bacterial proteomics: from sample preparation to database. *Methods Enzymol.* 358, 207-27.

Deiwick, J., Rappl, C., Stender, S., Jungblut, P.R., and Hensel, M. 2002 Proteomic approaches to Salmonella pathogenicity island 2 encoded proteins and the SsaAB regulon. *Proteomics* 2, 792-9.

Gatlin, C. L., Kleemann, G. R., Hays, L. G., Link, A. J., and Yates, J. R. 1998. Protein identification at the low femtomole level from silver-stained gels using a new fritless electrospray interface for liquid chromatography-microspray and nanospray mass spectrometry. *Anal. Biochem.* 263, 93-101.

James, P. 1997 Protein identification in the post-genome era: the rapid rise of proteomics. *Quart. Rev. Biophys.* 30, 279-331.

Kricka, L. J., Schmerfeld-Pruss, D., and Edwards, B. 1991. Chemiluminescent assay of enzymes using proenhancer and pro-anti-enhancers. *J. Biolumin. Chemilumin.* 6, 231-8.

Valaskovic, G. A., Kelleher, N. L., and McLafferty, F. W. 1996. Attomole protein characterization by capillary electrophoresis-mass spectrometry. *Science*, 273, 1199-202.

Wahl, J. H., Goodlett, D. R., Udseth, H. R., and Smith, R. D. 1993. Use of small-diameter capillaries for increasing peptide and protein detection sensitivity in capillary electrophoresis-mass spectrometry. *Electrophoresis*, 14, 448-57.

KEYWORDS: Protein, biosignatures, biothreat, detection

A04-T011

TITLE: Morphology and Composition of Nanomaterials Based on Laser Microplasma Spectroscopy

TECHNOLOGY AREAS: Materials/Processes, Weapons

OBJECTIVE: To develop an innovative technique for the determination of the chemical composition of nano-scale particles of military interest that is based on laser microplasma spectrochemistry. Techniques such as Laser Induced Breakdown Spectroscopy (LIBS) offer the possibility of establishing a complete chemical composition inventory of various materials. However, traditional LIBS is currently not able to operate on the 20-200 nm dimensions and thus innovative approaches are necessary to bring LIBS performance from the low micrometer length scale to the nanometric region.

DESCRIPTION: The military is conducting numerous aggressive R&D programs on various nano-scale materials for applications in biology, materials, electronics, chemistry, and physics. Areas such as nanocomposites, molecular electronics, molecular motors, self-assembled nanoenergetics, and nanobiotechnology are just a few examples of important new application areas that will benefit the warfighter. A major obstacle to making progress on the nanoscale is the lack of powerful diagnostic techniques that work effectively on the nanoscale for the determination of the morphology and chemical composition of nanomaterials. Laser ablation and plasma formation offer an intriguing possibility to accomplish chemical analysis on the nanoscale. Laser ablation sampling is the generation of a vapor-phase aerosol using a pulsed high-power laser beam focused on a sample surface. Any sample (solid, liquid, organic, inorganic, opaque, transparent, conducting, insulator, etc.) can be laser ablated. There are no sample-size or shape requirements; bulk samples as well as individual particles can be directly analyzed. The spatial properties of the laser beam allow the identification of heterogeneity in the sample. For example, a single laser pulse on a sample can be used to study surface contamination or it can be used to clean the surface in order to study underlying composition. Many nanoparticle production processes involve the production of particles in flowing reactant streams. Laser ablation offers the potential for in-situ monitoring of size and composition of the nanoparticles. As nanotechnology becomes more prominent in our society, the ability to analyze samples on the nanoscale will become important. Laser ablation sampling can provide this capability, and the possibility of nanoscale resolution has been demonstrated. Several studies have investigated the use of NSOM (near-field scanning optical microscopy) and AFM (atomic force microscopy) for ablating samples with nanometer-diameter resolution. Significant research is needed in this area to develop laser ablation on the nanoscale – the referenced papers demonstrate that the technology is possible, with data having been obtained using LIBS for aerosol particles in the 200 nanometer size range. An aggressive goal is the development of an analytical system capable of single shot measurements of properties on the nanometer scale.

PHASE I: Design, develop and breadboard an opto-electronic system for the study of surfaces, particularly nanocomposites and nanoenergetics and particles of these and other nanoscale materials at nanometer scale using laser ablation and plasma formation analysis. Determine through analysis and limited demonstration the system temporal, spatial and species resolution limits. Define optimized opto-electronic system.

PHASE II: Develop and demonstrate optimized opto-electronic system. Setup a laboratory system, demonstrate its temporal, spatial and species resolution capabilities for a range of candidate nanostructured systems (to be determined in consultation with the Army).

PHASE III DUAL USE APPLICATIONS: Development of a commercializable/marketable nanomaterial analysis system. For research laboratory use, this could be a straightforward development based on the laboratory system created for Phase II. For more turnkey and portable applications, a system could be developed using solid state laser technology and ruggedized components.

What is the explicit civilian use?

REFERENCES:

1. Y. Ding, R. Micheletto, H. Hanada, T. Nagamura, S. Okazaki, Rev. Sci. Instrum. 73 (2002) 3227.
2. D. Kossakovski, J.L. Beauchamp, Anal. Chem. 72 (2000) 4731.
3. B. Dutoit, D. Zeisel, V. Deckert, R. Zenobi, J. Phys. Chem. B 101 (1997) 6955.

KEYWORDS: Spectrometry, plasma, laser, ablation, composition analysis, nano-particle, nano-structure

A04-T012

TITLE: High Power Mid-Wave Infrared (MWIR 3-5 Mmicron) Semiconductor Lasers

TECHNOLOGY AREAS: Chemical/Bio Defense, Sensors, Electronics

OBJECTIVE: Design, construct, and test a small lightweight laser module (preferably uncooled or thermoelectrically cooled above -40C) operating in the 3-5 microns operating with continuous wave output. The developed system should be based on compound semiconductor technology and enable easy system integration. Sensors that use infrared lasers can be then developed to find chemical traces of explosives, weapons, narcotics and other contraband associated with enemy activities.

DESCRIPTION: Remote sensing of toxic chemical agents is an extremely important and challenging problem in today's environment. Many of the chemical species of interest to the Army/DoD (as well as many other gases and chemicals) have characteristic signatures in the 3-5 micron regime. Potential chemical weapon detection applications would include nerve and blister agents such as TABUN (GA), SARIN (GB), SOMAN (GD), VX (VX), S-MUSTARD (HD), LEWISITE (L), PHOSGENE (CG), HYDROCYANIC ACID (AC), CYCLOSARIN (GF). Other potential applications in the area of explosive detection include RDX, PETN, TNT, Semtex, NG, HMX, Ammonium Nitrate and others. Lastly, in the area of drug detection potential applications would be detection of Cocaine, Heroin, THC (Cannabis) Methamphetamine, and others. However, there are very few high power uncooled lasers that can be used for such sensing applications. A new emitter is desired that can be used for remote sensing application via spectral fingerprinting, ie. matching the absorption spectra for the unknown to a library of signatures. Typically the strongest vibrational modes are in the mid-infrared portion of the spectrum. To this end, high efficiency lasers (which would constitute active sensing) based on mature III-V [1,2,3], IV-VI, or other semiconductor technologies are needed. The requirements on the lasers are high output powers (~100 mW/laser or more), good efficiency and preferably room temperature operation. For higher power applications where one or several bars reaches a Watt or more of power, special attention to heat transfer and packaging will be considered as part of the work.

PHASE I: Design and show the feasibility of a high performance electrically injected laser in the 3-5 microns range operating continuous-wave at room temperature with a power of >20 mW in order to show feasibility.

PHASE II: Package the laser into a compact module, which could be used in remote sensing applications. The objective of this phase should be to deliver a compact laser module prototype with a total output of >0.5 W at room temperature (i.e. 10 lasers @ 50mW/laser).

PHASE III Dual Use Applications: Demonstrate a working remote sensing system, which can detect a specified toxic agent simulant. Alternative applications include IR countermeasures and various lidar system applications. Civilian applications include pollution monitoring, factory-process control, toxic-gas detection, and human breath analysis for medical diagnostics. Another possible application for civilian/DoD is wireless communications.

REFERENCES:

1. E. A. Pease, L. R. Dawson, L. G. Vaughn, P. Rotella, and L. F. Lester, "2.5-3.5 μ m optically pumped GaInSb/AlGaInSb multiple quantum well lasers grown on AlInSb metamorphic buffer layers," J. Appl. Phys., 93, 3177, 2003.
2. Andrew P. Ongstad, Ron Kaspi, Joseph R. Chavez, Gregory C. Dente, Michael L. Tilton, and Donald M. Gianardi, "High-temperature performance in ~4 μ m type-II quantum well lasers with increased strain," J. Appl. Phys. 92, 5621, 2002.
3. J.S.Yu, S. Silken, A. Evans, L. Doris, and M. Razeghi, "High-power continuous-wave operation of a 6 micron quantum-cascade laser at room temperature," Applied Physics Letters, 83, 2503, 2003.

KEYWORDS: III-V and IV-VI semiconductors, laser, chemical warfare agents, toxic industrial chemical

A04-T013

TITLE: Biologically Inspired Acoustic Direction Finding for Soldiers

TECHNOLOGY AREAS: Ground/Sea Vehicles, Sensors, Electronics

OBJECTIVE: The objective of this research is to develop a compact, lightweight, wearable, biologically inspired integrated sound source localization system to be used by individual soldiers for increasing their situational awareness of the auditory battlefield environment (e.g. sound source directions, source spectra). It is anticipated this technology would provide an added

level of force protection by allowing a soldier to quickly determine and respond to enemy threats in the battlefield (e.g. sniper location). In later phase developments, it is envisioned the system would provide a network capability in the field to enable collaborative computation of the auditory scene.

DESCRIPTION: An acoustic direction finding system could be developed with current technology by employing free-field microphone sensor arrays and traditional signal processing techniques (e.g. Multiple Signal Classification). In simple terms, this method works because the time delays (i.e. frequency-dependent phase-differences) associated with plane waves arriving at different microphone elements can be used to estimate the direction of arrival of a sound signal's source. The performance of this approach can yield satisfactory results in some application areas, but recent developments have shown these methods can be improved upon by additional processing of the sound signal. It has been known for quite some time that in nature, the ability to localize sound sources is greatly enhanced by binaural processing that takes into account the frequency-dependent difference in phase as well as the log-intensity difference between the ears. Integrated sensor/processing systems based on biological mimicry of binaural hearing have the potential for increased performance over traditional frequency-dependent phase-difference only approaches. However, one obstacle for using log-intensity difference properties is the accurate modeling (i.e. transfer function) required of the sensor environment. Current research indicates progress has been made to overcome this obstacle, and that it may now be possible to employ binaural processing for this application. In laboratory settings, recent work in mathematical modeling of sound propagation around a spherical head has lead to the design of a system that captures effectively the biological principle of localization using both inter-aural phase difference and inter-aural level difference [1], [2]. Incorporation of inertial information from the sensor-array rotation (i.e. acoustic flow) further enhanced this capability by allowing the directional ambiguities caused by symmetry to be resolved. Despite this progress, further challenges and risks associated with this technology remain: (a) problems of interference from multiple sound sources with overlapping spectral components; (b) the need to provide significant sensing and signal processing capabilities in a lightweight integrated wearable system; (c) the need to fuse acoustic information with motion sensed by inertial or other means; (d) the problem of effective presentation of the results of the computations to the soldier. This research will support the development of a soldier based sound source localization system that overcomes the aforementioned problems.

PHASE I: Demonstrate through simulation and laboratory testing a prototype device to characterize the 3-D sound source environment. Identify deficiencies and paths for improvements to deployment such as soldier integration, potential networking improvements, ease of use, robustness, fabrication, reparability, system cost, durability, weight and endurance. Characterization of overall system performance will include but not be limited to directional sensitivity, bandwidth limitations, signal selectivity, minimum detectable signal, susceptibility to counter measures, and noise floor.

PHASE II: The first milestone of Phase II will be to design, build and demonstrate a stand-alone hardware/software prototype system in a dynamic unknown environment. The system envisioned must be a fully operational device for use by a single soldier. To meet the second milestone for phase II, the system will be modified to simulate operation in a networked environment. A team of software agents will be networked with the stand-alone system for performance evaluation purposes. System robustness and survivability will be measured to assess the performance of the networked system with and without countermeasures.

PHASE III: Design, build, and test a fully operational prototype system for a small platoon of no less than five (5) soldiers. The system will have full network capability to provide enhanced information of the complete sound source environment. Examples of commercial application opportunities include use by rescue workers to locate victims in severe environments such as: fire victims in smoke filled buildings, the lost or injured hikers in wilderness areas during darkness, heavy fog, or winter white-out conditions.

REFERENCES:

1. A. A. Handzel and P. S. Krishnaprasad (2002) "Bio-mimetic sound source localization", IEEE Sensors Journal 2(6), pp. 607-616.
2. A. A. Handzel, S. B. Anderson, M. Gebremichael and P. S. Krishnaprasad (2003) "A bio-mimetic apparatus for sound source localization", to appear, Proceedings of the 42nd IEEE Conference on Decision and Control, IEEE, Maui, Hawaii.
3. B. Baertlein, R. Moses (2003), "Personnel Detection Technology Assessment: Final Report", Report #743391-2, US Army Research Office, Durham, NC.
4. J. Blauert (1997) Spatial Hearing, 2nd ed., MIT Press, Cambridge.
5. X. J. Eicke, J. Lavery (1999) "Distributed Microsensing: Devices, Networks and Information Processing", Strategic Assessment Report, Army Research Lab.
6. J. Weng and K. Y. Guntchev (2001) "Three dimensional sound localization from a compact non-coplanar array of microphones using tree-based learning", Journal of the Acoustical Society of America, 110(1), pp. 310-323.

KEYWORDS: Binaural hearing, portable lightweight acoustic localization, portable adaptive acoustic arrays, acoustic direction finding

A04-T014

TITLE: High-Resolution Near-Field Probe System for Microwave Circuit and System Design and Analysis

TECHNOLOGY AREAS: Materials/Processes, Sensors, Electronics

OBJECTIVE: Develop a high-resolution near-field probe system for microwave circuit and system design and analysis. Develop software for converting the near-field data to coupling and far-field radiation models.

DESCRIPTION: Coupling and radiation are effects that traditionally have been associated with high-frequency analog circuits and systems. As digital clock frequencies increase, coupling and radiation become issues for high-speed digital circuits and systems as well. These effects are typically included late in the design cycle, and often empirical fixes are the only available solution. This topic seeks to develop sophisticated capability for vector measurement of electric and magnetic fields with high resolution, close to the surface of planar circuits and within the packaging of modules, closely integrated with software for converting the near-field measurements to coupling and far-field radiation models.

The developed technology must be capable of measuring both magnitude and phase of electric and magnetic fields within 25 microns of the surface of the circuit under test. The technology must have high resolution, preferably below 100 microns. The physical size and aspect ratio of the probe tip must allow measurement at full accuracy and resolution both within the die cavities of microwave packages and over the full topography of multi-chip modules. Sensitivity should be appropriate for the measurement of fields surrounding low-power radio frequency analog and high-speed digital circuits. The measurement bandwidth must be high enough to capture not only the fundamental frequency of a digital signal (such as a 10 Gbps data stream), but also at least several harmonics of the signal, potentially to above 100 GHz. Waveform acquisition time must be compatible with production-rate testing of parts and circuits.

In conjunction with the hardware, software must be developed that can convert the near-field measured data into coupling and far-field radiation data that can be used to extract component and circuit models. These models must be compatible with current computer aided design and engineering (CAD/CAE) software packages so that the designer has a useable tool for evaluating system inter-component coupling and electromagnetic compatibility/electromagnetic interference (EMC/EMI) performance without resorting to post-facto empirical methods.

This will enable significant reduction in the design cycle time of communication and radar systems for the Objective Force, and for commercial cellular phones and other types of portable devices.

PHASE I: Demonstrate feasibility for vector measurement of electric and magnetic fields with high resolution, close to the surface of planar circuits and within the package boundaries of chips and multi-chip modules. Demonstrate feasibility for a software package for converting near-field measurements to coupling and far-field radiation models. Deliver design data for the hardware and specifications for the software, along with a constructive work plan to achieve proof of concept for the integrated system in Phase II.

PHASE II: Construct and demonstrate a working prototype of an integrated system based on Phase I results. Measure fields over sample microwave devices and deliver coupling and far-field models compatible with current CAD/CAE software to relevant DoD laboratories.

PHASE III DUAL USE APPLICATIONS: Near-field measurement coupled with appropriate software can become a key enabling technology for virtual prototyping of mixed signal integrated circuits, multi-chip modules, and complete systems by providing radiation and coupling models of system components that can be integrated into computer automated design and engineering (CAD/CAE) packages. The resulting technology will enable significant reduction in the design cycle time of communication and radar systems for the Objective Force, and for commercial cellular phones and other types of portable devices.

REFERENCES:

- 1) J.F. Whitaker, Kyoung Yang, R. Reano, and L.P.B. Katehi, "Electro-optic field-mapping as a diagnostic tool for microwave circuits and antenna arrays," in International Topical Meeting on Microwave Photonics, 2002, pp. 73- 76.
- 2) Yaqiang Wang and M. Tabib-Azar, "Microfabricated near-field scanning microwave probes," in IEDM '02 Digest, 2002, pp. 905 – 907.
- 3) K. Slattery and Wei Cui, "Measuring the electric and magnetic near fields in VLSI devices," in 1999 IEEE International Symposium on Electromagnetic Compatibility, Vol. 2, 1999, pp. 887-892.

KEYWORDS: Near-field, electric field, magnetic field, vector measurement, high resolution

A04-T015

TITLE: Terahertz-Frequency Quantum-Dot (THz QD) Lasers for Sensing & Communications

TECHNOLOGY AREAS: Materials/Processes, Sensors, Electronics

OBJECTIVE: To design, build and demonstrate a new class of coupled quantum-dot (QD) laser sources that offer unprecedented opportunities for realizing higher output powers and efficiencies at terahertz (THz) frequencies through the revolutionary use of solid-state micro-disk cavity architectures.

DESCRIPTION: The envisioned optical-emission device should build upon recent scientific breakthroughs in nano-materials engineering that allow for the efficient coupling of emission from quantum-dot (QD) systems. Specifically, self-assembly of QD systems has been demonstrated to be naturally amenable to integration through the use of whispering-gallery micro-disk cavities. The performance increases and cost-effective advantages enabled through the development of THz-QD Laser electronics will have important impact to military applications such as THz-frequency remote/point spectroscopic detection of chemical and biological agents, THz-frequency imaging of weapons and explosions, space/covert communications and high-speed signal processing. At present, the U.S. Army actively supports innovative research efforts in the area of high-frequency electronics that seek new and revolutionary approaches for realizing significant performance enhancements at THz frequencies. Obviously, the successful implementation of a robust and cost-effective technology base at these very high-frequencies and data-rates offers a number of important strategic advantages. However, state-of-the-art electronic device technology must be advanced significantly before THz-frequency technology can be realistically and successfully applied towards important sensing and communication applications that relevant to military defense. The two most significant and long-standing challenges for fielding THz-frequency systems are the development robust sources (i.e., output power, efficiency, tunability) and the very high cost of the fabricating and integrating the hardware. While a number of novel approaches are currently under development, it is clear that revolutionary advances in electronics will be required before a full spectrum dominance of the THz regime (i.e., ~ 0.3 to 10 THz) is achieved. A recent breakthrough in use of micro-disk cavities [1] for integration of coupled QD systems suggests that an optical emission source may now be a viable and practical approach for achieving coherent power generation at very long wavelengths. This new work is significant because it suggests an innovative approach for overcoming the major problems (i.e., competing parasitic processes and poor material quality) that have plagued conventional solid-state Lasers in the far IR regime. For example, to date the most successful demonstration of an optical source at THz frequencies is the quantum Cascade laser [2] which utilizes 1-D quantum confinement to tune transition energies and rates. However, respectable output powers (e.g., ~ 1 mW) have only been achieved above approximately 3 THz and at very low operating temperatures (i.e., ~ 40 K). Alternatively, the utilization of self-assembled QD systems (with 3-D confinement) allow for engineering intersubband transitions [3] and leads to reduced absorption losses introduced by free-carrier, phonon, Auger and intervalence processes. Furthermore, and most importantly, the effective engineering of these QD systems only becomes viable through the use of the high-quality micro-disk cavities that were only recently demonstrated.[4]. Specifically, the micro-disk architecture was shown to reduce material costs and processing time and to simplify the fabrication steps. Therefore, a focus research and development effort is proposed to enable the full demonstration of a THz QD laser that is robust, cost-effective and practically useful for future sensing and communication applications. This proposed STTR project is very complimentary to an existing MURI program on "THz-Frequency Sensing Science and Electronic Technology," as it defines completely new developmental work in optics-based source technology.

PHASE I: The first phase of the program should establish realistic and effective designs for coupled QD laser systems for both the near IR and submillimeter-wave regimes, utilize narrow bandgap semiconductor materials and intersubband engineering approaches to define a practical micro-disk based architecture. Initial efforts should address the general feasibility of QD laser operation within the near IR wavelength and identify potential bottleneck problems for extending the concept to lower frequencies. This initial phase of the project should also establish a firm base of insights into the optimum use of materials and quantum structures.

PHASE II: In the second phase of the program, advanced design and scaling techniques should be employed to facilitate a prototype demonstration of a QD laser at submillimeter-wave frequencies (i.e., ~ 1 THz). This phase of the project should apply advanced modeling to optimize a QD prototype design within the context of micro-disk cavity structures. Detailed measurements of device output power and overall efficiency should also be a component of this effort.

PHASE III DUAL USE COMMERCIALIZATION: The optical technology developed under this topic will define a new innovation in very high-frequency sources. This last phase of the program can be used to assess operational capability under practical applications of the technology. The resulting emission devices have important relevance to medical applications for the microscopic interrogation of biological characteristics and chemical function. Specific civilian applications include the use of spectroscopic sensing and imaging of cancer and for the monitoring of biological processes. This new technology can also enable the characterization of other materials of interest such as electronic materials and explosives. The very high components developed under this effort also have implications to signal processing and communication systems.

REFERENCES:

- [1] G. S. Solomon, M. Pelton and Y. Yamamoto, Phys. Rev. Lett., 86, 3903 (2001).
- [2] M. Rochat, et. al., Appl. Phys. Lett., 81, 1383 (2002).
- [3] W. Fang, J. Y. Xu, A. Yamilov, H. Cao, Y. Ma, S.T. Ho and G. S. Solomon, Opt. Lett., 27 948 (2002).
- [4] G. S. Solomon, Z. Xie and M. Agrawal, "Terahertz Emission using Quantum Dots and Microcavities," Chapter 6 in Terahertz Sensing Technology, Vol. II (World Scientific, Singapore, 2003).

KEYWORDS: Quantum Dots, Micro-cavities, Nano-materials, Optical emission devices, THz sources

A04-T016

TITLE: Smooth, Piecewise-Polynomial Terrain Representation Using Nontraditional Metrics

TECHNOLOGY AREAS: Information Systems, Ground/Sea Vehicles

OBJECTIVE: Develop software for terrain representation by smooth (C1-smooth or more) piecewise polynomials on irregular triangulations using nontraditional metrics.

DESCRIPTION: Strategic and tactical decisions based on computed estimates of terrain dramatically impact performance of Army and DOD assets. Currently, open and urban terrain is most often represented by piecewise planar surfaces on triangulated irregular networks (TINs) because such surfaces fit within current hardware constraints and do not have extraneous oscillation. However, people and platforms on TINs often do not have accurate intervisibility (lines of sight) because of the flat-surface nature of the facets that make up the TINs. When virtual vehicles are run across TINs, the flatness of the surface inside each triangle and the discontinuity in slope as one goes from one triangle to the next create nonphysical behavior. Preventing these problems within a TIN framework requires fine triangulations and therefore storage and manipulation of large amounts of data. This results in large computing time and reduced zoom-in/out capability. The result is that TIN terrain skins often perform poorly when included into higher-level modeling and simulation. Recent experience of 1SG Rudy Romero, highlights some of these issues with the current TIN-based software [1].

The conceptual superiority of using smooth surfaces for representation of terrain has long been recognized. However, previously available smooth-surface techniques such as conventional polynomial and rational splines, radial basis functions and wavelets require too much data, too much computing time, too much human interaction and/or do not preserve shape well. In particular, conventional smooth splines are plagued by extraneous, nonphysical oscillation. There is an urgent need for smooth, data-compressed representation of terrain without nonphysical oscillation. Recent work indicates that using nontraditional (non-L2, that is, non-"root-mean-square") metrics, including the Hausdorff metric [2] and the L1 metric [3], can increase the accuracy and/or efficiency of both piecewise planar surfaces and smooth piecewise polynomials on irregular triangulations. This project focuses on combining smooth piecewise polynomials on irregular triangulations with approximation in nontraditional metrics.

PHASE I: Determine one or more nontraditional (non-L2, non-"root-mean-square") metrics that can be used to generate representations of terrain. Justify this/these metric(s) on the basis of satisfying one or more militarily relevant goals in terrain representation, such as accuracy of line of sight. Design smooth (C1-smooth or more) piecewise polynomials on irregular triangulations and determine the ability of these piecewise polynomials to approximate terrain optimally in this/these metric(s). Determine one or more algorithms for calculating these piecewise polynomials from point-cloud elevation data (not elevation data that has been rectified to a latitude-longitude grid) and demonstrate reliability (convergence and accuracy) of this/these algorithm(s). Plan the modules and flowchart for a software system that uses this/these algorithm(s).

PHASE II: Develop a prototype software system to calculate smooth piecewise polynomials on irregular triangulations from point-cloud elevation data using the non-traditional metric(s) and algorithms identified in Phase I. Carry out validation and verification of this software using natural and urban terrain data. Carry out computational comparisons of this software system with one or more currently available system, such as DYN-TACS, Janus (old and new), ModSAF and Bresenham using criteria such as accuracy, computing time and storage required. Identify limitations of the prototype system and determine whether these limitations are due to fundamental technical barriers. Carry out a demonstration of the prototype system.

PHASE III DUAL USE APPLICATIONS: In Phase III, the prototype software system should be adapted to various military and civilian situations where accurate, real-time terrain visualization is needed. Accurate, real-time battlefield visualization, calculation of viewshed from an arbitrary location, fly-through and zoom-in/zoom-out are primary military needs. In civilian situations, these same issues are important, perhaps with less emphasis on real time, for geospatial databases, city/area planning, drainage control and entertainment.

NOTE: The terrain surfaces to be considered throughout this project are univalent terrain skins. Multivalent terrain (overhangs,

bridges, layers of parking decks, insides of buildings, etc.) need not be considered in this project.

REFERENCES:

[1] Romero, ISG Rudy, "Lessons Learned during Afghanistan Deployment", <http://www.squad-leader.com/romero.htm>.

[2] Sendov, B., Hausdorff approximations. Kluwer, 1990.

[3] Champion, D.C. and Lavery, J.E., "Line of sight in natural terrain determined by L1-spline and conventional methods," in Proc. 23rd Army Science Conf. (December 2002), Department of the Army, Washington, DC (2002), OP-09, <http://www.asc2002.com/summaries/o/OP-09.pdf>.

KEYWORDS: Piecewise polynomial, point cloud, smooth, terrain, triangular irregular network

A04-T017

TITLE: High Confidence Multimodal Biometric System

TECHNOLOGY AREAS: Information Systems, Biomedical, Human Systems

OBJECTIVE: The objective of this STTR is to design and develop a high confidence multimodal biometric recognition system.

DESCRIPTION: Accurate personnel identification and verification have gained significant attention after the 9.11 attack. Biometric identification refers to matching an unknown human subject's biometric data to a specific record by searching a database (which may contain a large amount of biometrics records), so that the subject's identity can be discovered. Biometric verification uses the subject's biometric data to match his/her previously captured record in a database in order to determine whether the subject is truly the person he/she claims to be.

Biometric identification and verification involves an enrollment stage and a verification stage. During the enrollment stage, the biometrics system captures the subject's biometric signatures and saves them as the subject's biometric record. During the verification stage, the subject's biometric data is captured again and then matched against the stored record(s).

Biometrics based identification and verification have been promoted as one of the most promising technologies for achieving high confidence identification and verification [1, 2]. An effective and accurate identification system improves our capability in identifying potential terrorists. Using biometrics based access control to restricted physical or virtual spaces is the most reliable mean to secure government or private industry's confidential or classified secrets.

Unfortunately, biometrics based access control system has not been widely deployed, partially due to the variation in accuracy. The captured biometric data may be subject to various degradations during the initial enrollment stage and the subsequent verification stage. For example, in the case of facial image based recognition, the subject's facial image may experience various kinds of distortion such as smear, blur, or shift during capturing. These degradations lead to an increase in false accept and false reject rate.

A multimodal system, which combines the decisions made by a number of independent biometric measurements, has two clear advantages [3, 4, 5, and 6]:

1) Accuracy improvement by reducing false rates

The fusion of multimodal biometric data combines knowledge from several forms of biometric data, instead of just relying on a single form. As a result, degradation to a single-modal biometric data has a much less impact on the overall accuracy of identification or verification.

2) More robust in fraud prevention.

Since multiple types of biometric data are used in making an identification or verification decision, it will be much harder for a potential intruder to successfully masquerade different types of biometric data at the same time.

There are many forms of biometric recognition. Three most often used forms include facial image matching, iris matching, and finger print matching.

This STTR aims at developing an advanced multimodal biometric recognition system. A successful implementation must develop advanced technologies in the following areas:

1) Improvement in biometric data capturing

New technologies are needed to improve the biometric data capturing process. In addition, data degradation correction method is highly desirable. The improvement in biometric data quality will lead to a more accurate result [7, 8].

2) Effective multimodal biometric data fusion.

For a multimodal biometric system, effective data fusion needs to be developed so that the multimodal biometric data can be integrated intelligently in order to make a highly accurate decision [3, 5]. This is the most critical part of this STTR.

To summarize, the overall goal of this STTR is to develop a system that can provide a much higher accuracy in terms of low crossover error rate. In addition, the system needs to support two typical operations 1) high volume low security identification and verification 2) high security low volume identification and verification.

PHASE I:

- a. Select two biometric modalities (e.g., face and fingerprint) and appropriate testing data set for investigation.
- b. Develop feature recognition algorithms for the two selected biometrics and develop fusion method to combine the recognition information provided by the two modalities. Carry out experiment on both synthetic data and actual human biometric data. Compare the verification result to that generated by a single modality system. Report the comparison result.
- c. Demonstrate the advantages of multimodal biometric system vs. a single modality system.

PHASE II:

- a. Extend Phase I(b) efforts to allow for an increased number of biometric modalities.
- b. Develop a working prototype recognition system (both software and hardware), which can capture biometric data from a human subject and uses the captured biometric data for identification and verification.

PHASE III (DUAL USE COMMERCIALIZATION POTENTIAL):

Biometric recognition for high secure access is important to both military and commercial community. Successful demonstration of the developed technologies in a working system (both software and hardware) should address different types of applications ranging from low security high volume applications such as accessing ATM machines to high security low volume applications such as admission control to a military central command and control room. In the low security high volume case, cost management and system throughput are the main requirement. On the other side, high security low volume system needs to have a high confidence in verification accuracy and provides effective spoofing prevention.

REFERENCES:

1. J. G. Daugman, "High confidence visual recognition of persons by a test of statistical independence," IEEE Trans. Pattern Anal. Machine Intell., Vol.15, No. 11, pp. 1148-1161, 1993.
2. A. Jain, L. Hong, S. Pankati, R. Bolle, "An Identity-Authentication System Using Fingerprints," Proceedings Of The IEEE, Vol. 85, 1365-1388, 1997.
3. A. Ross and A. K. Jain, "Information Fusion in Biometrics", Pattern Recognition Letters, Vol. 24, Issue 13, pp. 2115-2125, September, 2003.
4. A. K. Jain and A. Ross, "Learning User-specific Parameters in a Multibiometric System", Proc. International Conference on Image Processing (ICIP), pp. 57-60, Rochester, New York, September 22-25, 2002.
5. A. Ross, A. K. Jain, and Jian Zhong Qian, "Information Fusion in Biometrics", Proc. 3rd International Conference on Audio- and Video-Based Person Authentication (AVBPA), pp. 354-359, Sweden, June 6-8, 2001.
6. L. Hong, A. Jain and S. Pankanti, "Can Multibiometrics Improve performance?", Proceedings AutoID'99, Summit, NJ, Oct 1999, PP. 59-64.
7. M. Savvides, B.V.K. Vijaya Kumar and P. Khosla "Face verification using correlation filters," Proc. Of the Third IEEE Automatic Identification Advanced Technologies, 56-61, Tarrytown, NY, March 2002.
8. J. G. Daugman, "High confidence visual recognition of persons by a test of statistical independence," IEEE Trans. Pattern Anal. Machine Intell., Vol.15, No. 11, pp. 1148-1161, 1993.

KEYWORDS: Multimodal biometrics, verification, recognition, identification, information fusion, access control

A04-T018

TITLE: Rapid Assessment of Individual Soldier Operational Readiness

TECHNOLOGY AREAS: Biomedical, Human Systems

OBJECTIVE: The objective is to develop a hierarchical series of molecular biomarkers for the rapid assessment of a soldier's physiological status and operational readiness. The individual becomes the biosensor.

DESCRIPTION: Individuals deployed to forward areas and combat zones are subject to a wide range of physiological stressors that can degrade combat readiness and performance. These include fatigue, nutrition, sustained physical activity, fear, sustained attention, environmental chemicals, and unusual pathogens, to name a few. New biotechnological techniques in the post-genomic era allow the rapid assessment of an individual's metabolic profile at any given time, allowing an evaluation of both long-term effects on health, as well as current state of readiness. A lethal or non-lethal response yields very little information for the level of effort. Efforts to characterize the vast middle ground of biological processes, between survival and death, have yielded a bounty of information and understanding. Central to these developments is the understanding that all biological responses are initially expressed at the molecular or subcellular level. At this level one can discriminate between protective and degenerative effects or responses. The level of response and the extent to which these biochemical indicators or biomarkers influence higher order functions is indicative of the severity of exposure. Biomarker responses are rapid and can be determined in situ yielding integrative responses under actual field conditions. Some examples of biomarkers include: DNA Damage and adducts, Cytochrome P-450, Stress Proteins, Vitellogenin, Lysosomal Destabilization. For example, Reactive Oxygen Species (ROS) are generated during periods of high metabolic rates associated with strenuous activity and in response to tissue injury as would be endemic in combat situations. ROS cause damage to membrane lipids, proteins, and DNA.

PHASE I: A range of biomarkers for human stress responses to a variety of physiologic insults will be identified. These should include, but are not limited to, genomic, proteomic and metabolic markers.

PHASE II: The potential of biochemical biomarkers depends on how they stand-up to simple criteria. In Phase II this rigour and robustness will be determined including chemical specificity of response, biological specificity, time of manifestation, permanence of response, variability of response, linkage to higher level manifestations, field application, and developmental status of the method. The goal of the biochemical biomarker approach is to develop a hierarchical series of sensitive molecular measures that will allow the rapid determination of the individual's general level of challenge and then progressively establish the character of the stimuli to which the individual is responding. Parameters for an in situ assay will be established and the biomarker data limited to standard measures of physical and cognitive performance. The final deliverable will be the development of functional test kits with capabilities for rapid analysis and the ability to handle complex responses to various environmental stimuli and to discriminate between benign and non-benign entities with greater sensitivity and resolution.

PHASE III COMMERCIALIZATION: There are numerous applications such as evaluations of athletic performance, monitoring workers in industrial settings, triage in the hospital following a biological or chemical attack, personalized medicine, and nutrigenomic

REFERENCES:

Genetic Biomarker References:

- Chiou CC, Chang PY, Chan EC, Wu TL, Tsao KC, Wu JT. Urinary 8-hydroxydeoxyguanosine and its analogs as DNA marker of oxidative stress: development of an ELISA and measurement in both bladder and prostate cancers. *Clin Chim Acta*. 2003 Aug; 334(1-2): 87-94.
- Haiman CA, Stampfer MJ, Giovannucci E, Ma J, Decalo NE, Kantoff PW, Hunter DJ. The relationship between a polymorphism in CYP17 with plasma hormone levels and prostate cancer. *Cancer Epidemiol Biomarkers Prev*. 2001 Jul; 10(7): 743-8.
- Lin CC, Wu HC, Tsai FJ, Chen HY, Chen WC. Vascular endothelial growth factor gene-460 C/T polymorphism is a biomarker for prostate cancer. *Urology*. 2003 Aug; 62(2): 374-7.
- Medeiros R, Moraes A, Vasconcelos A, Costa S, Pinto D, Oliveira J, Carvalho R, Lopes C. Linkage between polymorphisms in the prostate specific antigen ARE1 gene region, prostate cancer risk, and circulating tumor cells. *Prostate*. 2002 Sep 15; 53(1): 88-94.
- Ross JS, Fletcher JA, Linette GP, Stec J, Clark E, Ayers M, Symmans WF, Pusztai L, Bloom KJ. The Her-2/neu gene and protein in breast cancer 2003: biomarker and target of therapy. *Oncologist*. 2003; 8(4): 307-25.

Protein Biomarker References:

- Ariazi EA, Clark GM, Mertz JE. Estrogen-related receptor alpha and estrogen-related receptor gamma associate with unfavorable and favorable biomarkers, respectively, in human breast cancer. *Cancer Res*. 2002 Nov 15; 62(22): 6510-8.
- De La Monte SM, Wands JR. The AD7c-NTP neuronal thread protein biomarker for detecting Alzheimer's disease. *J Alzheimers Dis*. 2001 Jun; 3(3):345-353.
- Hampel H, Goernitz A, Buerger K. Advances in the development of biomarkers for Alzheimer's disease: from CSF total tau and Abeta (1-42) proteins to phosphorylated tau protein. *Brain Res Bull*. 2003 Aug 15; 61(3): 243-53.
- Hlavaty JJ, Partin AW, Shue MJ, Mangold LA, Derby J, Javier T, Kelley S, Stieg A, Briggman JV, Hass GM, Wu YJ. Identification and preliminary clinical evaluation of a 50.8-kDa serum marker for prostate cancer. *Urology*. 2003 Jun; 61(6): 1261-5.
- Kennard ML, Feldman H, Yamada T, Jefferies WA. Serum levels of the iron binding protein p97 are elevated in Alzheimer's disease. *Nat Med*. 1996 Nov; 2(11): 1230-5.
- Lehrer S, Diamond EJ, Stagger S, Stone NN, Stock RG. Serum insulin level, disease stage, prostate specific antigen (PSA) and Gleason score in prostate cancer. *Br J Cancer*. 2002 Sep 23; 87(7): 726-8.

- Luftner D, Possinger K. Nuclear matrix proteins as biomarkers for breast cancer. *Expert Rev Mol Diagn.* 2002 Jan; 2(1): 23-31.
- Ma BB, Poon TC, To KF, Zee B, Mo FK, Chan CM, Ho S, Teo PM, Johnson PJ, Chan AT. Prognostic significance of tumor angiogenesis, Ki 67, p53 oncoprotein, epidermal growth factor receptor and HER2 receptor protein expression in undifferentiated nasopharyngeal carcinoma-a prospective study. *Head Neck.* 2003 Oct; 25(10): 864-72.
- Monte SM, Ghanbari K, Frey WH, Beheshti I, Averbach P, Hauser SL, Ghanbari HA, Wands JR. Characterization of the AD7C-NTP cDNA expression in Alzheimer's disease and measurement of a 41-kD protein in cerebrospinal fluid. *J Clin Invest.* 1997 Dec 15; 100(12): 3093-104.
- Reynolds MA, Kirchick HJ, Dahlen JR, Anderberg JM, McPherson PH, Nakamura KK, Laskowitz DT, Valkirs GE, Buechler KF. Early biomarkers of stroke. *Clin Chem.* 2003 Oct; 49(10): 1733-9.
- Wehbi NK, Dugger AL, Bonner RB, Pitha JV, Hurst RE, Hemstreet GP 3rd. Pan-cadherin as a high level phenotypic biomarker for prostate cancer. *J Urol.* 2002 May; 167(5): 2215-21.
- Yousef GM, Diamandis EP. Expanded human tissue kallikrein family--a novel panel of cancer biomarkers. *Tumor Biol.* 2002 May-Jun; 23(3): 185-92.

KEYWORDS: Human performance, Sustainability, Mobility

A04-T019

TITLE: Tactical Biorefinery for Forward Fuel Production

TECHNOLOGY AREAS: Ground/Sea Vehicles, Materials/Processes

OBJECTIVE: The objective is to design a tactical field bio-refinery for expeditionary operations in austere environments. The bio-refinery would be designed to capitalize on the unique military circumstances of these types of operations in terms of its design, type of biomass input and fuel output. The overall objective is to provide timely fuel for critical initial operations while reducing logistical overhead.

DESCRIPTION: The need for timely availability of fuel during forced entry or expeditionary operations is a critical Army logistical requirement. Current logistics doctrine relies on high-overhead and costly methods should local fuel resources not be available. Further, the Total Army Analysis clearly showed that much of the fuel utilized during operations is consumed by stationary equipment such as small generators, cook burners, and other devices, rather than large combat vehicles or aircraft. These conditions imply that new advances in biotechnology related to biomass fuel production may have an important role in bridging the gap for availability of fuel during critical time periods and in austere environments. The new approaches made possible by genetically modified organisms, enzymes and alternative bioproduction methods may provide the necessary break-through means to design a tactical fuel production facility for special purpose use, analogous to our current inventory of Reverse Osmosis Water Purification Units.

PHASE I: Identify a promising biomass-to-fuel paradigm for military circumstances during expeditionary operations. Identify an appropriate input stream, processing technology, and output stream. Supporting models to demonstrate production capacity and operational context may suggest an initial prototype tactical biorefinery.

PHASE II: Phase II will focus on the design of a prototype tactical biorefinery and include physical development of the fundamental bioprocessing technology. Initial derivation of packaging, field use and location, and alternative biofeedstock will be identified and developed.

PHASE III COMMERCIALIZATION: Environmentally friendly and non-fossil fuel systems for energy may provide an attractive alternative to small or large businesses who recycle energy and energy laden waste material. A small biorefinery which can effectively reduce the cost of waste disposal and removal while simultaneously providing an offsetting fuel value would be an attractive end-item in a number of agricultural and manufacturing industries. The fundamental tactical biorefinery could be tuned to a variety of industrial groups and unique circumstances as a model class.

REFERENCES:

- Clements, L.D., S.R. Beck, and C. Heintz. 1983. Chemicals from biomass feedstocks. *Chem. Engr. Prog.* 79:59-62,
- Landucci, R., B. Goodman, and C. Wyman. 1994. Methodology for evaluating the economics of biologically producing chemicals and materials from alternative feedstocks. *Appl. Biochem. Biotech.* 45-46.
- Lynd, L.R: Cushman, J.H.; Nichols, R.J. Wyman, C.E. (1991) "Fuel Ethanol from cellulosic Biomass." *Science.* 251 (49999): pp 1318-1323.
- Morris, D. and I. Ahmed. 1992. The carbohydrate economy: Making chemicals and industrial materials from plant matter, The Inst. for Local Self Reliance, Washington, DC.
- SERBEP. 1998. World's first commercial biomass-to ethanol plant. SERBEP Update, Southeastern Regional Bioipmass Energy Program, Tennessee Valley Authority, Muscle Shoals, AL.
- Van Dyne, D.L., M.S. Kaylen, and M.G. Blasé. 1998. The economic feasibility of converting lingo-cellulosic feedstocks into

ethanol and higher value chemicals. Draft Report prepared for the National Ethanol Research Institute, administered by the Consortium for Plant Biotechnology Research, Inc. and the Missouri Division of Energy, University of Missouri, Dept. Agricultural Economics.

KEYWORDS: Fuel, Power, Biorefinery

A04-T020

TITLE: Metabolomic Evaluation of Combat Personnel for Optimum Fitness and Performance

TECHNOLOGY AREAS: Biomedical, Human Systems

OBJECTIVE: Develop and validate analytical platform of metabolic indicators and predictors of soldier health and mission performance capabilities as predicates for tailoring dietary regimens to individual metabolic profiles and task requirements.

DESCRIPTION: Future soldiers and defense force personnel must be capable of maintaining optimum health and mission performance within hostile and physically challenging environments which may far exceed the physical and mental demands experienced during the normal course of training. The army's focus on an "Objective Force" with revolutionary advances in soldier-centered capabilities will depend on significantly enhancing soldier health and performance as much as, if not more than, improving soldier equipment and battlefield technology. The evolving techniques of biotechnology in the postgenomic era can provide the necessary tools to allow a combat soldier to operate at peak levels over extended time in the many and varied environments within which s/he may find him/herself. One of the focus areas genomic technology offers is optimization of a soldier's health through determination and (and development) of a dietary regimen that is tailored to an individual's unique genetic make up—an area termed nutrigenomics as measured by the tools of metabolomics. Knowledge of an individual's metabolic profile may revolutionize the ability of dietary prescriptions to deliver health benefits through food in the same way that knowledge of genomics holds the promise of revolutionizing the prescription of pharmaceuticals to treat disease states based on individual genomic profiles.

The health of individuals, however, requires more than just genomic tools. This tool set must be expanded and similar principles applied to understand functional proteomics and metabolomics. The genomics revolution is having a major impact on nutrition intervention research that will result in diets and functional foods that maximize the health and performance of each individual. The tools of metabolomics will provide many of the parameters in making this a viable component in optimizing the health and performance ceiling of the individual soldier. Although metabolomics is still in its infancy, it has already been used to identify the function of genes, describe the effects of toxicological, pharmaceutical, nutritional and environmental interventions, and to build integrated databases of metabolite concentrations across human and research animal populations. Metabolomics provides nutrition science with an invaluable tool for determining the distributions of metabolite concentrations in humans, the relationship of these metabolite concentrations to stress and disease, and the extent to which diets and nutritional supplements can target and modulate metabolite concentrations correlated with optimum health and performance.

PHASE I: Phase I shall consist of a front-end analysis to identify and select a set of orthogonal metabolite profiles and define a suite of manual and mental tasks that discriminate individual differences in metabolic profiles before, during and after task demands. The feasibility of measuring metabolic parameters, dietary interventions selected to specifically effect metabolic change and the selection of individual tasks shall be demonstrated and documented in a Phase I report.

PHASE II. Metabolite profiles from large cohorts of individuals will be correlated with performance criteria and other indicators of optimum health. Advances in high-throughput analytic chemistry and computing technologies will be employed to create a comprehensive database of metabolic indicators from several subsets of metabolites, including lipids and organic acids. In Phase II, an integrative database of metabolites will be developed from both the general population and individuals selected for measuring metabolic profiles x task x time x diet. The current concept of measuring single biomarkers must be expanded in multidimensional space to 1) provide a comprehensive profile of metabolite measurements through parallel analyses, 2) obtain measures of the metabolic profile of individuals over time rather than simply in the fasted state, and 3) integrate these metabolic profiles with genomic, expression, and proteomic databases. At the conclusion of Phase II, a metabolic profiling process shall be delivered which defines the major metabolic profiles that are predictive of health and performance outcomes in divergent tasks, the analytical technology required to most rapidly obtain the profiles and a cost analysis of the aggregate test requirements.

PHASE III: With identification of indicator metabolites and metabolic profiles that predict degrees of general health and performance capabilities, databases of metabolome-based profiles can be extended for application in developing expert systems for screening health and performance baselines in many sub-groups of individuals for general health, disease states and performance in high stress situations (e.g., police, firemen, athletes, , air traffic controllers, etc...). The establishment of baseline metabolic profiles will also stimulate the emerging field of nutrigenomics in tailoring dietary intake to address metabolic deficiencies or improve individual metabolic efficiency and/or task performance.

REFERENCES:

Gavaghan CL, Holmes F, Lenz E, Wilson ID, Nicholson JK: An NMR-based metabonomic approach to investigate the biochemical consequences of genetic strain differences: application to the C57BL10J and Alpk:ApfCD mouse. FEBS Lett 2000, 484:169-174.

German JB, Ward RE and Dillard CJ. Bioactives in milk. Current Opinion in Clinical Nutrition and Metabolic Care 2002; S(6):653-658.

German JB, Roberts M-A, Fay LB and Watkins SM. Metabolomics and individual metabolic assessment: the next great challenge for nutrition. J Nutr. 2002 Sep;132(9):2486-7.

Holmes E, Antti H. Chemometric contributions to the evolution of metabonomics: mathematical solutions to characterising and interpreting complex biological NMR spectra. Analyst. 2002 Dec;127(12):1549-57.

Krauss R. Triglycerides and atherogenic lipoproteins: rationale for lipid management. Am J Med 1998;105:58S—62S.

Walsh MC, Berden JA, Brindle KM, Kell OB, Rowland et al.: A functional genomics strategy that uses metabolome data to reveal the phenotype of silent mutations. Nat Biotech 2001, 19:45-50.

German JB, Roberts MA, Watkins SM. Genomics and metabolomics as markers for the interaction of diet and health: lessons from lipids. J Nutr. 2003 Jun;133(6 Suppl 1):2078S-2083S.

Watkins SM, Hammock BO, Newman JW, German JB: Individual metabolism should guide agriculture toward foods for improved health and nutrition. Am J Chin Nutr 2001, 74:283-286.

Watkins SM and German JR. Towards the implementation of metabolic assessment of human health and nutrition Curr Opin Biotechnol. 2002 Oct;13(5):512-6.

Watkins, SM, Reifsnader PR, Pan HJ, German JR and Leiter EM. (2002) Lipid metabolomewide effects of the peroxisome proliferator-activated receptor γ agonist rosiglitazone. J Lipid Res. 2002 Nov;43(11):1809-17.

Waters NJ, Holmes F, Williams A, Waterfield Ci, Farrant RD, Nicholson JK: NMR and pattern recognition studies on the time-related metabolic effects of α -naphthylisathiocyanate on liver, urine, and plasma in the rat: an integrative metabonomic approach. Cheni Res Toxica~2001, 14:1401 -1 41 2.

KEYWORDS: metabolomics, metabolic profiles, nutrigenomics,

A04-T021

TITLE: Hazardous Vapor Collection and Concentration for Spectral Sensing

TECHNOLOGY AREAS: Chemical/Bio Defense, Materials/Processes

OBJECTIVE: Develop and evaluate novel substrate materials for propitious application as solid phase extraction (SPE) substrates for hazardous organic vapors such as chemical warfare agents (CWAs) and other volatile organic compounds (VOCs) with optical properties amenable to infrared and Raman spectroscopic interrogation. Such materials would be notionally employed in air monitoring sensors that interrogate the SPE surface by reflection-absorption or diffuse reflectance and/or with a Raman source.

DESCRIPTION: Chemical warfare agents present a significant threat to Future Combat Systems and Homeland Defense operations. The Department of Defense is developing and evaluating the next generation of chemical and biological sensor technologies for early warning protection of potentially exposed personnel. Optical spectroscopic methods such as infrared and Raman spectroscopy provide unique spectral fingerprints of organic compounds, facilitating the unambiguous identification of CWAs and other toxic industrial chemicals; however, detection of trace vapors is a challenge for these methods. Materials research is needed to develop SPE substrates that can collect and concentrate organic vapors onto a surface that is "spectroscopically benign" in that it either transmits or reflects mid infrared (radiation in the wavelength range from 2-25 microns) and Raman excitation radiation (typically a laser operating at a single wavelength in the ultraviolet through the near infrared region). No material is optically transparent across such a broad range of wavelengths, but many metallic materials afford excellent reflectivity across much of the entire electromagnetic spectrum. Metals make poor SPE substrates because of the absence nanoporous structures in the conventional metallic construct. Many metal oxides afford relatively benign diffuse reflectance substrates across much of the mid infrared region, but likewise do not typically form nanoporous structures for adsorption of organic vapors. Modern materials science presents a host of tools that may prove helpful in developing the optimal SPE substrate for infrared and Raman spectroscopy. Metals and metal oxides are routinely prepared as nanoparticles of controlled geometric scale. Such materials can be sintered or manufactured into mesoscale structures. As an added benefit, both surface-

enhanced infrared (SEIR) and surface-enhance Raman spectroscopy (SERS) has been reported on materials comprised of nanoparticulate silver and gold.

PHASE I: Phase I shall consist of a comprehensive phenomenology study and a series of proof-of-principle experimental demonstrations of both the optical properties and SPE (as well as SEIR and SERS as applicable) performance of a series of candidate materials. The product of the Phase I effort will be a detailed feasibility study including protocols for manufacturing and processing the SPE materials and detailed characterizations of the materials including porosity and optical/spectral diffuse reflectance measurements.

PHASE II: A systematic series of experiments shall be performed to screen a discursive set of metal and metal oxide constructs (as well as any other material compositions deemed appropriate for this application from the Phase I study) for suitability as SPE substrates for SEIR and SERS sensing of organic vapors. The propitious substrate would ideally be fabricated in the form of a microporous membrane or a fiber filter with nominal submicron porosity on the mesoscale and nanometer porosity on the microscale. Such materials could be directly employed as air filtration media that can simultaneously be monitored with infrared and/or Raman spectroscopy while collecting and concentrating particulate matter by virtue of the mesoscale pores and organic molecules by virtue of the SPE nanoscale pores. At the completion of the Phase II effort, a prototype air sampler that collects and concentrates particulate and vapor phase organic compounds to solid phase substrate compatible with infrared or Raman reflection mode spectroscopic interrogation will be manufactured and delivered.

PHASE III: The technology developed in Phase II will either be licensed to a sensor manufacturer or the performer will partner with a sensor manufacturer for the development of an inexpensive commercial sensor based on infrared and/or Raman spectroscopy.

REFERENCES:

- Ding, Y. and Erlebacher, J. (2003) Nanoporous Metal Architectures with Controlled Multimodal Pore Size Distribution. J. Am. Chem. Soc. 125, 7772–7773.
- Hartstein, A., Kirtley, J.R., and Tsang, J.C. (1980) Enhancement of the infrared absorption from molecular monolayers with thin metal overlayers. Phys. Rev. Lett. 45, 201-204.
- Kellner, R., Mizaikoff, B., Jakusch, M., Wanzenböck, H.D, and Weissenbacher, N. (1997) Surface-enhanced vibrational spectroscopy: a new tool in chemical IR sensing? Appl. Spectrosc. 51, 495-503.
- Priebe, A., Fahsold, G., and Pucci, A. (2001) Surface enhanced infrared absorption of CO on smooth iron ultrathin films. Surface Science 90. 482-485.

KEYWORDS: Nanotechnology, nanoporous, surface-enhanced Raman, surface-enhanced infrared, solid phase extraction, chemical warfare agent, spectral sensor, air monitor

A04-T022

TITLE: Novel Nano-Structures for Multiplexed Micro-Array

TECHNOLOGY AREAS: Materials/Processes, Sensors

OBJECTIVE: Develop a multiplexed assay array for the hand-held assay format. Combines 4 to 6 multiple agents detection on a single ticket.

DESCRIPTION: Hand-held lateral flow immunoassay is the standard format for DoD biological agent sensing. They are compact, easy to use, and require no power source. The standard format provides single agent detection on one hand-held “ticket”. The JSAWM program recently conducted a “feasibility” demonstration for multiple agent detection on a single “ticket”. Further work is need to extend the demonstration to 4 to 6 agents on a single ticket and demonstrate optimization and scale-up potential with a path to commercialization. It is desirable for the multiplex assay to either maintain or exceed current sensitivity performance in the JSAWM program.

The multiplexed assay will allow for rapid screening and detection of multiple agents simultaneously. It will decrease the logistical burden of soldier-in-the-field by reducing the number of tests that need to be conducted to screen an area for possible BW contamination. It will reduce the cost per assay run.

PHASE I: Design and optimize a 4-plex assay that does not have background streaking, cross bleeding, or flow problems and maintains current JSAWM sensitivities limits. Demonstrate feasibility for scale up and produce tickets suitable for live agent testing and ROC curve development. Total number of required tickets will be determined, but will not exceed 10,000. Conduct additional reagent screening and determine feasibility for 4, 6 and 10-plex microarray format.

PHASE II: Produce microarray quantities for technology characterization. Live agent testing is necessary for the best characterization and performance measurement, but may not be within available resources at this phase. ROC curve analysis is

required. Further decrease background signal from reagent streaking. Phase II will culminate in a prototype demonstration.

PHASE III DUAL USE APPLICATIONS: Demonstrate scale-up and production capabilities. Conduct testing with live agent and complex backgrounds; performance analysis methods shall be consistent with Phase II.

Joint Chemical and Biological Agent Water Monitor

Homeland Defense first responders, water utilities

EPA Homeland Security Research Center has expressed an interest in this platform technology. They may have other target agents they wish to incorporate.

Environmental monitoring

REFERENCES:

1. R. Yin, M. Bratcher, A. Jenkins, R. Hydutsky, R. Cheng, H. D. Durst, P. Emanuel, G. Hagnauer, "Dendrimer-based Alert Ticket: A Novel Nanodevice for Bio-Agent Detection", Polymeric Materials Science & Engineering, 84, 856 (2001).
2. R. Yin, et. al, "Methods of Using Nanomanipulation for Enhancing Bioassay Performance" U.S. Patent Pending (1999).
3. R. Yin, J. Jensen and H. Durst, et. al "Nanomanipulation-based Handheld Assays: Detection of B. Anthracis Spores and Ricin from Various Water Sources" JSAWM Report on February 10, 2003 (JSAWM Web Folder).
4. Emanuel, Peter A.; Dang, Jessica; Gebhardt, Joan S.; Aldrich, Jennifer; Garber, Eric A. E.; Kulaga, Henrieta; Stopa, Peter; Valdes, James J.; Dion-Schultz, Amanda . Biosens. Bioelectron., 14(10-11), 751-759 (2000)
- 5.. Grunow, R; Splettstoesser, W.; McDonald, S.; Otterbein, C; O'Brien, T.; Morgan, C.; Aldrich, J.; Hofer, E. ; Finke, E-J. ; and Meyerl, H. ; Clin Diagn Lab Immunol. 7 (1) 86-90 (2000).
6. Warsinke A, Benkert A, Scheller FW, Fresenius J Anal Chem 366, 622 (2000)
7. Vetcha, Srinivas; Wilkins, Ebtisam; Yates, Terry; Hjelle, Brian, Talanta, 58(3), 517-528 (2002)
8. "CDC Health Advisory: Hand-Held Immunoassays for Detection of Bacillus anthracis Spores." October 18, 2001 <http://www.bt.cdc.gov/DocumentsApp/Anthrax/10182001HealthAlertPM/10182001HealthAlertPM.asp>
9. "Use of Onsite Technologies for Rapidly Assessing Environmental Bacillus anthracis Contamination on Surfaces in Buildings." CDC MMWR Vol 50 Number 48. December 7, 2001. <http://www.cdc.gov/mmwr/PDF/wk/mm5048.pdf>
10. "Approved Tests for the Detection of Bacillus anthracis in the Laboratory Response Network." <http://www.bt.cdc.gov/DocumentsApp/Anthrax/ApprovedLRNTests.asp>

KEYWORDS: Hand-Held-Assay, multiplex, microarray, nanotechnology, lateral flow immunoassay

A04-T023

TITLE: Use of Shape Memory Alloys for Structural Energy Dissipation in Extreme Loading Events

TECHNOLOGY AREAS: Materials/Processes

OBJECTIVE: Develop structural framing connection elements that can be used in Department of Defense (DoD) buildings to dissipate energy from earthquake ground motions and from accidental or intentional explosions that may occur near buildings, using shape memory alloy (SMA) materials.

DESCRIPTION: In regions of high seismic activity, new DoD buildings must be designed to withstand the effects of damaging earthquakes. Worldwide, new multistory DoD buildings must also be designed to resist progressive collapse when explosions destroy load-bearing column or wall elements. Requirements similar to those for new buildings are already in effect for renovations of existing DoD buildings in seismically active areas, and will soon (FY 04) be in effect for the prevention of progressive collapse in existing multistory DoD buildings. The traditional methods of strengthening by using more steel and concrete are expensive and limit functional use of buildings. SMA materials have been developed over the past 15 years that possess unique abilities to undergo large magnitude (7+%) strains that can be recovered. This ability to recover very large strains without damage results in the ability to dissipate large amounts of strain energy from extreme loading events such as explosions and earthquakes. Early development and application of SMA materials focused on very small diameter wire specimens, limiting their use in applications where large loads occur, such as in buildings. In the past 6-8 years, SMA materials, principally Nitinol (Nickel Titanium Naval Ordnance Laboratories), have become machinable in larger diameter sizes. Limited testing has been performed on specimens of approximately 5 cm diameter. It is now possible to use the larger SMA's in structural reinforcement

and connections where large ductility and energy dissipation, without failure, can make structures more survivable under extreme loading conditions. This effort will first characterize the material properties of SMA materials in larger specimen sizes – it is not clear yet that the same properties as those in wire size specimens exist. Size effects on energy dissipation capacity and strain rate sensitivity will be emphasized. The characterization will also explore alternatives to Nitinol for large specimen sizes. Following the material characterization, design concepts for applying SMA's in structural connection and reinforcement details will be developed. Typical applications will include connections of exterior cladding to superstructures, beam-column moment-resisting connections, concrete reinforcement, and diaphragm-to-superstructure connections. The design concepts will then be tested in the laboratory environment under dynamic loading conditions. Successfully tested designs will be engineered for field application and marketability.

PHASE I: Determine availability of SMA materials in large specimen sizes (> 3 cm diameters). Characterize material behaviors of SMA's as functions of material specimen size, with emphasis on energy dissipation capacity, fatigue behavior, sensitivity to high strain rates, and capability to recover large permanent strains through mechanical, electrical, or thermal means. Determine capacity for use as post-tensioning systems. Develop structural reinforcement and connection details that utilize the material behaviors that are found.

PHASE II: Develop and demonstrate via laboratory and/or field testing prototype designs of structural systems that use SMA's to dissipate earthquake or explosion-induced energy. Develop computer modeling techniques that are usable in the commercial sector for structural analysis, to support engineering design.

PHASE III DUAL USE APPLICATIONS: This system as developed will be directly transferable to the civilian sector, both other government agencies and private entities, for the design of buildings, bridges, and other structures. In addition, the development of larger specimen sizes holds the potential for further military applications in armor applications, bridging, aircraft, and spacecraft.

REFERENCES:

- Duerig, T. W., et al, "Engineering Aspects of Shape Memory Alloys," Butterworth Heinemann, London, UK, 1990.
- Epps, J. and Chopra, I., "Comparative Evaluation of Shape Memory Alloy Constitutive Models with Test Data," Proceedings of the 38th AIAA Structures, Structural Dynamics and Materials Conference and Adaptive Structures Forum, Kissimmee, FL, 1997.
- Funakubo, "Shape Memory Alloys," New York: Gordon and Bleach, 1987.
- Hess, G. W., "Cyclic Behaviour of Shape Memory Alloy Tendons and Steel Bolted T-Stub in Beam-Column Connections," Department of Civil and Environmental Engineering, Georgia Institute of Technology, 2000.
- Krumme, et al. "Structural Damping with Shape Memory Alloys: One Class of Devices," Smart Structures and Materials Conference, The International Society for Optical Engineering (SPIE), San Diego, CA, 1995.
- Liang, C., and Rogers, C. A., "Design of Shape Memory Alloy Springs with Applications in Vibration Control," Journal of Vibrations and Acoustics, ASME, Vol 115 (No. 1), pp. 129-135, 1993.
- Ocel et al, "High Damping Steel Beam-Column Connections Using Shape Memory Alloys," Proceedings of Seventh U.S. National Conference on Earthquake Engineering, Earthquake Engineering Research Institute, Boston, MA, July 2002.
- Ocel et al, "Full-Scale Testing of Nitinol-Based Semi-Rigid Connections," Proceedings of Twelfth European Conference on Earthquake Engineering, London, UK, September 2002.
- Whittaker, Andrew S., et al. (1995). "Structural Control of Buildings Response Using Shape Memory Alloys," USACERL Technical Report 95/22, US Army Corps of Engineers Construction Engineering Research Laboratories.

KEYWORDS: Shape Memory Alloys, Dynamic Loading, Energy Dissipation, Earthquake Loading, Progressive Collapse

A04-T024

TITLE: Artificial Oxygen Carrier Solution for Small Volume Resuscitation

TECHNOLOGY AREAS: Biomedical, Human Systems

OBJECTIVE: To design an intravenous artificial oxygen carrier, effective in small volumes (less than 100 ml), that can be used by medics in the field under extreme environmental conditions that provides resuscitation of severely hemorrhaged soldiers.

DESCRIPTION: Recent studies have demonstrated that rebleeding occurs following aggressive resuscitation back to normal blood pressure in the pre-hospital period with experimental subjects that have a vascular injury (1). In response to these findings, the military doctrine for battlefield resuscitation is changing, and casualties will only receive sufficient fluid resuscitation to maintain a level of consciousness. Many of the casualties will have low hematocrits, and it is possible that some casualties will have progressive shock under these conditions. In ongoing animal studies of low volume resuscitation for prolonged periods of time, the hematocrits have fallen to such a degree as to provide inadequate oxygen delivery. Hemoglobin-based oxygen carriers are under development but may be in limited supply if made from human hemoglobin, may have a blood-pressure raising ability due to the binding of nitric oxide that may dislodge clots, and may require special storage capability to prevent freezing or high temperatures.

It would be of great benefit to develop an artificial oxygen carrier that is small volume, lightweight, and stable across a wide range of temperatures. An example of a possible oxygen carrier is dodecafluoropentane (DDFP), which was originally successfully developed for use as an ultrasonic contrast medium. DDFP has a beneficial effect of carrying large quantities of oxygen to the tissues as the intravascular microbubbles pick up oxygen from the lungs, expand 150 times in volume (since its boiling point is 29 degrees C.) though remains smaller than a red blood cell, and then delivers oxygen to the tissues. Recent experiments in pigs have shown that hemorrhagic shock that is fatal in untreated controls is survivable in animals that have been treated with only 0.3 ml of DDFP emulsion/kg (2). Animal data indicate that 1 ml of DDFP in this form can support the entire oxygen consumption (300 ml O₂/min) of a resting adult person (normally provided by 5,000 ml of circulating blood). Moreover, since the microbubbles can be expected to equilibrate with all gases in the surrounding tissue they can be employed for transport of other gases than oxygen. For instance, it has been demonstrated in a pig model that combined with oxygen breathing, injection of the DDFP emulsion substantially enhances nitrogen washout from the tissues (3). This may offer an avenue for treatment or prevention of decompression sickness in divers and astronauts (during extravehicular activities).

PHASE I: This phase should result in a proof of concept of an artificial oxygen carrier that is effective in small volumes, stable at the temperature and pressure extremes experienced by soldiers (cold altitude of the mountains to heat of the desert), require no special handling or mixing, and is biocompatible.

PHASE II: This phase should result in a long term (at least 1 year), shelf-stable artificial oxygen carrier that can be demonstrated to be effective in the resuscitation in a lethal hemorrhage animal model. The mechanism of action of its beneficial effect should be ascertained as well as its pharmacological characteristics, such as half-life, tissue distribution, and excretion. It also must be demonstrated that it can be stored, transported and administered under temperature and ambient atmospheric conditions likely to be encountered in military field settings. Specifically, it must be demonstrated that the substance is effective even after storage at 50 degrees C. for 2 – 3 months simulating time in a medic's backpack while deployed. The substance should also be shown to be effective if it has been frozen (simulating storage in cold environment). It must be demonstrated that the substance will be effective when given at altitudes at which a soldier may be deployed.

PHASE III COMMERCIALIZATION: This artificial oxygen carrier would have immediate battlefield application and civilian trauma application to be used by paramedics in the field or on ambulances. This may particularly apply to rural or other delayed extraction situations where field blood supplies may be in short supply.

REFERENCES:

1. Sondeen, JL, Coppes, VG, and Holcomb, JB. Blood pressure at which rebleeding occurs after resuscitation in swine with aortic injury. J Trauma, 2003, May; 54(5 Suppl): S110-7..
2. Lundgren C., Bergoe G. and Tyssebotn I. Hemorrhagic shock in air breathing pigs treated with bubble-forming intravenous dodecafluoropentane emulsion. Artificial Blood, 11: 1, abstract F-1-4, 2003.
3. Lundgren C., Bergoe G.W. and Tyssebotn I. Tissue denitrogenation by microbubbles. Programs and Abstracts of Thirty-Fourth Annual Undersea and Hyperbaric Medical Society Scientific Meeting, 14-16 June 2001, San Antonio, Texas, Vol. 28 (Suppl.), Abstract 28.

KEYWORDS: Hemorrhagic shock, Resuscitation, Artificial oxygen carrier

A04-T025

TITLE: Automated Behavioral Health Triage

TECHNOLOGY AREAS: Biomedical, Human Systems

OBJECTIVE: Develop instruments that are sensitive to specific cognitive functional areas and organize the information into a logic-tree suitable for use in conjunction with or by incorporation into existing military cognitive-function test systems. The end product should provide concurrent and transparent analysis of individual test results and automatically configure a tailored battery of additional test modules relevant to functional areas noted as meriting additional testing. Technical risk exists in both selection of functional areas that cover broad cognitive domains but are sensitive and specific enough, by clustering or overlap, to identification of domain subsets relevant to specific cognitive dysfunction as well as in constructing a stand-alone instrument compatible with out-put features of cognitive-function test systems currently available to the military

DESCRIPTION: Advances in the development of specific tests of cognitive and behavioral performance permit insight into specific alterations in neuropsychological function and make possible application of triage techniques in this field. Measurement of alterations in cognition by specific tests provides the potential to compose additional, secondary sets (batteries) of more sensitive and specific tests that will reveal a more detailed view of performance-relevant cognitive functions at a specific point in time. Normative data for large populations is not currently available for precise comparison of individual performance with a larger population; thus specific categorization of individual performance compared to the general population is not practical. However, there is sufficient research literature regarding the correlation of specific test results related to functional

neuropsychological areas to provide a basis for determining significance of variations in individual tests. Patterns of performance deviations within or across multiple tests of common and key cognitive functional areas should provide information that permits more thorough analysis. Existing research provides both general understanding of typical cognitive performance characteristics and the repeated measure testing technology to create a longitudinal functional profile for a specific individual. Similarly, the results of adaptive, dual-level testing instrument will provide a more precise and objective means of determining the practical implications of impaired performance seen in a screening test battery. The testing instrument would thereby provide a means of triage related to specific performance areas that are heavily dependent on specific functional domains.

PHASE I: In Phase I, an assessment of the results of available and standard-of-care cognitive tests and a mapping of the relevance of results to specific functional cognitive and behavioral domains will be completed. Analysis of the influence of overlap of one or more tests to specific functional and cognitive domains will also be completed. A survey of pertinent literature linking key functional areas necessary for basic levels of cognitive performance will be completed. Analysis as to whether it is possible to determine minimal levels of function within each identified cognitive domain, as an indicator for initiating increased testing of a more specific neuropsychologically defined domain will be established, and a logic-tree will be produced that provides "test/no test" decision points will be created for use in Phase II development of the automated, simultaneous and transparent analysis of cognitive test results for determination of cognitive dysfunction and identification of areas of cognitive performance requiring more specific and sensitive testing.

PHASE II: In Phase II the prototype logic tree and methodology for validating its consistency developed in early portions of Phase II will be combined to receive input from selected off-the-shelf automated neuropsychological and cognitive performance test systems. The goal of the analysis of output data will be to provide an automatic selection of additional modules for testing functional areas in need of additional, more specific and sensitive testing. Test modules for more specific cognitive domains or domain subsets will be automatically selected, using the "test/no test" decision points of the logic-tree developed in Phase I and with reference to findings from prior and the current testing results. A prototype will be constructed and tested in a cohort of individuals selected from a population with objective neuropsychological assessments by qualified professionals. Care will be taken to include individuals from both the general population and from specific subpopulations where decline of neuropsychological or cognitive performance could be expected or has been noted. The expected product of this phase is a functional integration of the logic-tree analysis and module selection methodology with one or more currently available off-the-shelf automated tools or for use as a stand-alone means of objectively triaging individuals into categories for further, more specific cognitive testing, based on results of other standard-of-care methods.

PHASE III: The completed prototype will be integrated with available neuropsychological assessment tools and offered to transportation officials for evaluation in fatigue and sleep deprivation studies, to pharmaceutical firms engaged in determining the effect of specific drugs on cognitive function, to professionals interested in following progression and alteration of individual patient progress, and to the military for use in determining rapid triage of cognitive and neuropsychological function of individuals in operational environments. The completed tool will be useful for examination of effects of environmental conditions on cognitive performance and may be offered for preliminary clinical psychological and psychiatric testing and for use in monitoring patients such as those with head injury.

REFERENCES:

- Barr, W. B. (2003). Neuropsychological testing of high school athletes. Preliminary norms and test-retest indices. *Archives of Clinical Neuropsychology* 18(1): 91-101.
- Bendetto, J., Harris, W., and Goernert, P. (1995). Automated Neuropsychological Assessment Metrics (ANAM) performance stability during repeated cognitive assessments (Technical Report EPRL-TR-95-02). Mankato, MN: Mankato State University.
- Bleiberg, J., Garmoe, W., Cederquist, J., Reeves, D., and Lux, W. (1993). Effects of Dexedrine on performance consistency following brain injury: A double-blind placebo crossover case study. *Neuropsychiatry, Neuropsychology, & Behavioral Neurology* 6(4): 245-248.
- Bruggemans, E. F., Van de Vijver, F. J., and Huysmans, H. A. (1997). Assessment of cognitive deterioration in individual patients following cardiac surgery: correcting for measurement error and practice effects. *Journal of Clinical and Experimental Neuropsychology* 19(4): 543-559.
- Dikmen, S. S., Heaton, R. K., Grant, I., and Temkin, N. R. (1999). Test-retest reliability and practice effects of expanded Halstead-Reitan Neuropsychological Test Battery. *J Int Neuropsychol Soc* 5(4): 346-356.
- Farmer, K., Cady, R., Bleiberg, J., and Reeves, D. (2000). A pilot study to measure cognitive efficiency during migraine. *Headache* 40(8): 657-661.
- Heaton, R. K., Temkin, N. R., Dikmen, S., Avitable, N., Taylor, M. J., Marcotte, T. D., and Grant, I. (2001). Detecting change: A comparison of three neuropsychological methods, using normal and clinical samples. *Archives of Clinical Neuropsychology* 16: 75-91.
- Horton, A. M., Jr., and Sobelman, S. A. (1994). The General Neuropsychological Deficit Scale and Halstead Impairment Index: comparison of severity. *Percept Mot Skills* 78(3 Pt 1): 888-890.
- Jacobson, N. S., and Truax, P. (1991). Clinical significance: a statistical approach to defining meaningful change in psychotherapy research. *J Consult Clin Psychol* 59(1): 12-19.
- Kane, R. L., and Kay, G. G. (1992). Computerized assessment in neuropsychology: A review of tests and test batteries.

Neuropsychol Rev 3(1): 1-117.

McSweeney, A. J., R.I., N., Chelune, G. J., and Luders, H. (1993). "T Scores for change": An illustration of a regression approach to depicting change in clinical neuropsychology. *The Clinical Neuropsychologist* 7: 300-312.

Naylor, E., Penev, P. D., Orbeta, L., Janssen, I., Ortiz, R., Colecchia, E. F., Keng, M., Finkel, S., and Zee, P. C. (2000). Daily social and physical activity increases slow-wave sleep and daytime neuropsychological performance in the elderly. *Sleep*. 23(1): 87-95.

Rahill, A. A., Weiss, B., Morrow, P. E., Frampton, M. W., Cox, C., Gibb, R., Gelein, R., Speers, D., and Utell, M. J. (1996). Human performance during exposure to toluene. *Aviat Space Environ Med* 67(7): 640-647.

Temkin, N. R., Heaton, R. K., Grant, I., and Dikmen, S. S. (1999). Detecting significant change in neuropsychological test performance: A comparison of four models. *Journal of the International Neuropsychological Society* 5: 357-369.

Warden, D. L., Bleiberg, J., Cameron, K. L., Ecklund, J., Walter, J., Sparling, M. B., Reeves, D., Reynolds, K. Y., and Arciero, R. (2001). Persistent prolongation of simple reaction time in sports concussion. *Neurology*. 57(3): 524-526.

KEYWORDS: Neuropsychological testing, cognitive performance, behavioral performance

A04-T026

TITLE: GPS-Based Tracking System for Trauma Patients

TECHNOLOGY AREAS: Biomedical, Electronics

OBJECTIVE: To design a system to monitor the location of trauma patients during their pre-hospital care and within the trauma centers until their arrival in the operating suite.

DESCRIPTION: Large volume resuscitation can lead to increased bleeding and lower survival rates in patients with intrabdominal injuries. Limited small volume hypotensive resuscitation minimizes the risk of increased bleeding and decreases the volume of resuscitation fluid that must be carried by the medic (1). Hypotensive resuscitation is currently in use on the battlefield with promising results (2) but recent studies in animals suggest that improved resuscitation fluids may be needed if casualties are expected to remain hypotensive for prolonged periods of time (1). Long evacuation times are predicted in future engagements. The evacuation times were quite long in Somalia, and a similar situation may be expected in future battles because of more dispersed casualties. To address this problem, several new resuscitation fluids are under development or currently ready for clinical trial (3). However, there are many hurdles in conducting pre-hospital clinical trials in resuscitation. One of these hurdles is the inaccurate measurement of the time of critical events in the care of trauma patients. The time of injury is almost always unknown in trauma patients and transport times are only estimates (4). The delay until surgical intervention varies from center to center and it is dependent on the number of casualties arriving simultaneously to the trauma center or emergency department. Since these variables may greatly affect outcome, it is imperative that these times are accurately recorded. One method to accurately obtain these times is for the emergency responder to place a GPS based monitoring system on the trauma victim when he/she first arrives at the accident scene. Information from this GPS based system could be monitored at a central location and with the addition of transponders within the trauma centers and the surgical suites, most of the critical times could be accurately determined. Additional information is available for automobile accidents involving "smart cars" that transmit the initial call for help at the time of an accident. By merging the patient GPS data with the information from the "smart cars" monitored by the Department of Transportation, the time of injury can be accurately determined. Additionally an estimate of the severity of injury can be obtained from the car's maximal deceleration rate. By accounting for the variability induced by differences in the time of transport and time until surgery, it is expected that the clinical trials could be completed more quickly with fewer patients. This translates into the more rapid FDA approval for new resuscitation fluids. GPS based locators and transmitters are currently available from a number of sources (5) but the proposed system would require integration with in-hospital transponders. It should provide for a redundant and rigorous method of communication that would function at any location within the study area and would work in times of heavy use. Moreover the system should allow for easy integration with the data from the Department of Transportation, and easy integration with the study protocols.

PHASE I: This phase should be a proof of concept. GPS-locators should be developed or adapted from commercial products. These GPS-units ideally would be small enough to be worn as a wrist watch and provide sufficient battery power for 48 hours operation, by using intermittent duty cycles, or other means to accomplish power conservation while still providing reliable signal transmission to 100m (the location of the ambulance or transport vehicle). For phase I, 6-hour battery life is sufficient. The patient worn device should comply with the IEC standard for EMI immunity 60601-1-2(1993) or meet any applicable recent compliance standards appropriate to minimize the risk of electromagnetic interference with medical devices within the hospital setting (6). Low power transmission and care in the choice of transmission frequencies (7) will help to meet this requirement. An ambulance-based transponder will receive the patient information and retransmit it with sufficient power so that the signal can be received from any location in the study area. The transmission wavelengths for the transponder should comply with FCC regulations. The transmitted information should include not only patient identifier and location but also the location of the transponder. In this phase the transponder would only be required to use only one transmission frequency, and a cell phone transmission would meet this specification if there were broad phone coverage within the study area.

PHASE II: Battery life of the patient worn device should be extended to 48 hours. This phase should also include development of a monitoring system compatible with the Department of Transportation's "smart car" reporting system. The system should automatically link the "smart Car" information with the GPS-locators that co-localize with the car within two hours. The system should be able to handle up to one hundred simultaneous transmissions and display location and time of critical events from each patient. The transponders for this system should be capable of redundant or variable methods of transmitting the data (5,8) so that information could be obtained even if one communication system was inoperable or overloaded at the time of the incident. The system should be centrally located but displays and real-time data should be available at other locations through a secure web-based system. Deliverables should include 10 wristwatch transmitters, four in-hospital transponders for evaluation in the clinical trials, and a data display and analysis system. Documentation should be provided from the Safety Committee/EMC professional, of a level one trauma center within the study area specifying that the device meets their standards for electromagnetic compatibility and is considered safe for use within their trauma bays and surgical suites.

PHASE III DUAL USE APPLICATIONS: Dual use applications include epidemiological studies of trauma care, and most importantly this system could be used to assist in the response to a mass casualty. In the instance of a natural disaster the system could be used to detect "choke points" in the transportation of casualties, and to oversee the distribution of patients so that local level 1 trauma centers are not overburdened. Since the proposed system will be in almost constant use for trauma studies, it is more likely to work when needed for mass casualties. This averts a major logistic problem common to most mass casualty response systems that normally lie in storage until they are needed, i.e. intermittent limited testing. If the mass casualties are the result of a bombing, knowledge of the distribution of the patients could be critical if it is discovered, subsequent to the initial events, that the explosive device was contaminated (dirty bomb).

REFERENCES:

1. Dubick, M.A. and Atkins, J.L. (2003). Small volume fluid resuscitation for the far forward combat environment: Current concepts. *J. Trauma* 54 (5), S43-S45.
2. LTC Erin Edgar, 82nd Airborne Division Surgeon (2003) Quoted in "Iraqi Freedom Roundup" in *Mercury* 30(11), August.
3. Carrico, C.J., Holcomb, J.B., Chaudry, I.H., and the PULSE Work Group (2002). Scientific Priorities and Strategic Planning for Resuscitation Research and Life Saving Therapy Following Traumatic Injury: Report of the PULSE Trauma Work Group. *Shock* 17(3), 165-168.
4. Lerner, B., Billittier, A., Dorn, J., and Wu, Y. (2003). Is total out-of-hospital time a significant predictor of trauma patient mortality? *Acad. Emergency Medicine* 10 (9), 949-954.
5. Budinger, T. (2003). Biomonitoring with Wireless Communications. *Ann. Rev. Biomedical Engineering* 5, 383-412.
6. <http://www.fda.gov/cdrh/emc/emc-in-hcf.html>
7. <http://www.fcc.gov/oet/dockets/et99-255/>
8. <http://www.intel.com/update/contents/wi07031.htm>

KEYWORDS: Hemorrhagic Shock, Resuscitation, Trauma, GPS-locators, Trauma Systems, EMC/EMI, Electromagnetic Compatibility

A04-T027

TITLE: Development of Bioassays for Prion Infectivity Using Human, Deer, or Elk Cells

TECHNOLOGY AREAS: Biomedical

OBJECTIVE: Develop a human, deer, or elk cell culture model for prion propagation which can be used as a bioassay for detecting prions.

DESCRIPTION: There is significant need for better methods to detect prion-related diseases that cause transmissible spongiform encephalopathies (TSE). Current infectivity bioassays involve the use of mice or hamsters. A cell culture model for prion propagation could lead to the development of a reproducible model for studying the mechanism of prion infectivity and disease. Additionally, a cell culture model for prion propagation could be used as an assay for the screening of potential prion therapeutics and could replace the animal test with a more rapid and sensitive cell-based diagnostic assay.

Research will be directed toward the development of novel human, deer, or elk cell-based models for prion propagation. The cell model can consist of primary and/or engineered cell lines or co-cultures that have been optimized to support the propagation of prions. The inclusion of secondary cell types and/or other biological factors that support the purpose of the model is encouraged.

Methods that are both sensitive and specific for detecting prion infection in the cultured cells must also be identified. Collaborations to develop the cell model for prion propagation and the infectivity detection assay are encouraged. The test method developed must be sensitive, specific, reproducible, and timely. Innovative concepts are highly encouraged.

PHASE I. Select one species, either human, deer, or elk, for the development of cell lines. Create several novel cell lines from the selected species that support prion propagation at detectable levels. A sensitive and specific method to detect prion propagation in the cultured cells is essential to demonstrate the proof-of-principle.

A detailed and specific plan for access to cells and/or tissues for the selected species must be provided in the application. A detailed and specific plan for the tissue and types of cells that will be used, and how the cell lines will be developed must also be included. Alternative approaches should be discussed, and the selected approach justified. Potential technical problems should be identified and addressed.

Collaboration/subaward with a lab that has access to and capabilities in prion research is encouraged for the development of the detection assay.

The use of human cells and tissues and/or animal use will require approval by the appropriate USAMRMC regulatory board.

PHASE II: Using the Phase I cell culture(s), develop and validate a bioassay for detecting prions in tissues and body fluids. This bioassay must be sensitive, specific, and reproducible.

PHASE III: The commercialization potential of the resulting cell model and bioassay is high and is an important consideration in both the military and civilian environments. The assay system for detecting prions should be applicable to assessing the food and blood supply. Analysis of animals at the time of slaughter, screening of live animals, and early detection of prions in humans and animals, and blood products are several applications of this technology. Moreover, this assay technology will be important to the research study of prions. Proof of principle in Phase II should be sufficient to facilitate marketing of this assay to pharmaceutical or biotech companies possessing the capability of completing assay kit development and any required FDA approvals.

REFERENCES:

1. Ingrosso, L., Vetrugno, V., Cardone, F., and Pocchiari, M. Molecular diagnostics of transmissible spongiform encephalopathies. Trends in Molecular Medicine: 2002, 8:273-280.
2. Collinge, J. Prion diseases of humans and animals: Their causes and molecular basis. 2001, 24:519-50.
3. Prusiner, S. Prions. Proc. Natl. Acad. Sci USA. 1998, 95:13363-13383.

KEYWORDS: Prion diagnostics, prion propagation, infectivity bioassay, diagnostics, cell culture model, neural cell model

A04-T028

TITLE: Portable Cell Maintenance System for Rapid Toxicity Monitoring

TECHNOLOGY AREAS: Chemical/Bio Defense, Biomedical

OBJECTIVE: The objective is to develop a small, portable cell maintenance system for the transport, storage, and monitoring of viable vertebrate cells and tissues. Advances in this area are critical for transitioning laboratory-developed toxicity screening devices into field-deployable systems to identify potential health effects on deployed forces resulting from water-borne exposures to a wide array of toxic chemicals.

DESCRIPTION: As part of on-going research in the field of deployment toxicology, the U.S. Army Center for Environmental Health Research (USACEHR) is seeking new methods for providing rapid toxicity evaluation of water samples in field environments. Although vertebrate cell- and tissue-based toxicity sensors show considerable promise for this purpose, a major limitation has been transitioning sensors from laboratory to field environments. In particular, field toxicity sensors would benefit from the availability of a cell maintenance system (CMS) that would maintain vertebrate cell viability and sterility through transport, storage, and testing and be compatible with interfaces for acquisition and analysis of cell signaling data relevant to toxicity identification, e.g., optical (visible, fluorescent, or luminescent) or electrical (from electrically active cells). We are seeking innovative and creative research and development approaches that take advantage of recent technological advances in such areas as biocompatible materials and microfluidics to provide a portable system that will provide a self-contained source of viable vertebrate cells.

PHASE I: Conduct research to provide a proof of concept demonstration of a CMS capable of maintaining vertebrate cells and providing access to cell signaling information usable in a cell-based toxicity monitor. The concept will be original or will represent significant extensions, applications, or improvements over published approaches. Design considerations for a proof of concept demonstration are listed below. Although these considerations are based on a CMS including multiple cell/tissue cartridges and a mounting assembly for the cartridges to maintain appropriate environmental conditions, other designs providing

similar functionality are acceptable.

1. Each cell cartridge must have dimensions suitable for use in a hand-held device and be fabricated from biocompatible materials suitably inexpensive to be disposable.
2. The cell cartridge mounting assembly must allow rapid and robust insertion of the cell cartridge and while maintaining sterile fluidic interconnections.
3. The CMS must provide temperature control within 0.1 degrees C and should be constructed from materials capable of maintaining the pH of media using CO₂ gas through standard phosphate/bicarbonate buffering.
4. The CMS should provide pH and osmolarity monitoring of cell/tissue culture media.
5. The CMS must be capable of maintaining cell viability, environmental conditions, and sterility for a three-day demonstration period. Systems capable of maintaining more than one cell type are preferred.
6. The CMS should be designed to accommodate data acquisition for optical and/or electrical signals from cells and tissues.

PHASE II: Expand upon the Phase I proof of concept demonstration to construct a prototype CMS device. Minimize the size and logistical requirements of the CMS. Increase the length of time that vertebrate cells can remain viable and useful in the CMS to two weeks and provide the capability to withstand variable environmental conditions (e.g., temperature, humidity, shock and vibration). Demonstrate CMS capabilities for cell viability and cellular data acquisition under field-relevant conditions of transportation and use. Provide three CMS systems for further independent evaluation and testing.

PHASE III DUAL-USE APPLICATION: Integrate the cell cartridges from the CMS for use with vertebrate cell-based rapid toxicity monitoring systems that will evaluate the suitability of drinking water for deployed troops under field conditions. Field tests will involve shipping the CMS to Army field sites and testing the toxicity sensing capabilities. Given current on-going concerns regarding accidental or intentional contamination of water supplies, this technology will have broad application for water utilities as well as state and local governments. In addition, modular systems for maintaining vertebrate cell systems should be broadly usable for high-throughput screening of pharmaceutical products for efficacy and toxicity.

OPERATING AND SUPPORT COST REDUCTION (OSCR): Failure to rapidly identify toxic hazards in water may lead to health impairments during or after deployment, resulting in loss of readiness and increased medical costs. Rapid chemical detection capabilities are limited and do not address potential health hazards from exposure to industrial or agricultural chemicals soldiers could encounter during deployment as a result of damaged infrastructures, accidental spills, or hostile acts. The availability of a CMM will overcome a major obstacle to the use of vertebrate cells for rapid identification of acute toxic hazards in water, thus providing increased protection of deployed soldiers from health risks related to chemically-contaminated water.

REFERENCES:

Pancrazio J. 2001. Preface. *Biosensors and Bioelectronics* 16:427-428.

Pancrazio J, Whelan JP, Borkholder DA, Ma A, Stenger DA. 1999. Development and application of cell-based biosensors. *Annals of Biomedical Engineering* 27:697-711.

DeBusschere BD, Kovacs GTA. 2001. Portable cell-based biosensor system using integrated CMOS cell-cartridges. *Biosensors and Bioelectronics* 16:543-556.

KEYWORDS: Rapid toxicity identification, toxicity sensor, toxic industrial chemicals, cell maintenance system, cell cartridge